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Circle only 466888

From: Kim, Jennifer
Sent: Monday, October 06, 2003 9:50 AM
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Subject: ,I need to order these articles please.. 10/075718

1. Hellman, S. 1997. Principles of cancer management: Radiation therapy. In Cancer: Principles and Practice of Oncology, V.T.DeVita, S. Hellman &S.A.Rosenberg, Eds.: 307-332. J. B. Lippincott Co. Philadelphia, PA.

2. Rotman, M., H. Aziz & T.H. Wasserman. 1998. Chemotherapy and radiation. In Cancer: Principles and Practice of Radiation Oncology, C.A. Perez & L.W.Brady, Eds.: 705-722. J.B.Lippincott Co. Philadelphia, PA.

3. Mattern, M.R., G.A. Hofmann, F. McCabe, et al. 1991. Synergistic cell killing by ionizing radiation and topoisomerase I inhibitor topotecan (SK&F 104864). Cancer Res. 51: 5813-5816. year 1991

4. Chen., A.Y., P. Okunieff, Y. Pommier, et al. 1997. Mammalian DNA topoisomerase I mediates the enhancement of radiation cytotoxicity by camptothecin derivatives. Cancer Res. 57: 1529-1536.

5. Chen, A.Y., H. Choy & M.L. Rothenberg. 1999. DNA topoisomerase I-targeting drugs as radiation sensitizers. Oncology 13: 39-46.

Thanks,
Jennifer Kim 308-2232, 2D17
Art Unit 1617

STIC-ILL

10/6

From: Kim, Jennifer
Sent: Monday, October 06, 2003 9:50 AM
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466873

1. Hellman, S. 1997. Principles of cancer management: Radiation therapy. In Cancer: Principles and Practice of Oncology, V.T.DeVita, S. Hellman &S.A.Rosenberg, Eds.: 307-332. J. B. Lippincott Co. Philadelphia, PA.

2. Rotman, M., H. Aziz & T.H. Wasserman. 1998. Chemotherapy and radiation. In Cancer: Principles and Practice of Radiation Oncology, C.A. Perez & L.W.Brady, Eds.: 705-722. J.B.Lippincott Co. Philadelphia, PA.

3. Mattern, M.R., G.A. Hofmann, F. McCabe, et al. 1991. Synergistic cell killing by ionizing radiation and topoisomerase I inhibitor topotecan (SK&F 104864). Cancer Res. 51: 5813-5816.

4. Chen., A.Y., P. Okunieff, Y. Pommier, et al. 1997. Mammalian DNA topoisomerase I mediates the enhancement of radiation cytotoxicity by camptothecin derivatives. Cancer Res. 57: 1529-1536.

5. Chen, A.Y., H. Choy & M.L. Rothenberg. 1999. DNA topoisomerase I-targeting drugs as radiation sensitizers. Oncology 13: 39-46.

Thanks,
Jennifer Kim 308-2232, 2D17

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10/6

Fr m: Kim, Jennifer
Sent: Monday, October 06, 2003 9:50 AM
To: STIC-ILL
Subject: I need to order these articles please.. 10/075718

466881

1. Hellman, S. 1997. Principles of cancer management: Radiation therapy. In Cancer: Principles and Practice of Oncology, V.T.DeVita, S. Hellman &S.A.Rosenberg, Eds.: 307-332. J. B. Lippincott Co. Philadelphia, PA.

2. Rotman, M., H. Aziz & T.H. Wasserman. 1998. Chemotherapy and radiation. In Cancer: Principles and Practice of Radiation Oncology, C.A. Perez & L.W.Brady, Eds.: 705-722. J.B.Lippincott Co. Philadelphia, PA.

3. Mattern, M.R., G.A. Hofmann, F. McCabe, et al. 1991. Synergistic cell killing by ionizing radiation and topoisomerase I inhibitor topotecan (SK&F 104864). Cancer Res. 51: 5813-5816.

4. Chen., A.Y., P. Okunieff, Y. Pommier, et al. 1997. Mammalian DNA topoisomerase I mediates the enhancement of radiation cytotoxicity by camptothecin derivatives. Cancer Res. 57: 1529-1536.

5. Chen, A.Y., H. Choy & M.L. Rothenberg. 1999. DNA topoisomerase I-targeting drugs as radiation sensitizers. Oncology 13: 39-46.

Thanks,
Jennifer Kim 308-2232, 2D17

agl- RC 271. R3. P73 1998

agl
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VDD
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=> d his

     (FILE 'HOME' ENTERED AT 09:05:37 ON 06 OCT 2003)

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
     CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,
     EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF,
     MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 09:05:56 ON 06 OCT
     2003

     FILE 'REGISTRY' ENTERED AT 09:06:16 ON 06 OCT 2003
L1              1 S CAMPTOTHECIN/CN

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
     CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,
     EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF,
     MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 09:06:48 ON 06 OCT
     2003

=> s camptothecin (p) rebeccamycin
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'PTOTHECIN (P) REBECCAMY'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'PTOTHECIN (P) REBECCAMY'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
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PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'PTOTHECIN (P) REBECCAMY'
L2            168 CAMPTOTHECIN (P) REBECCAMYCIN

=> dup rem l2
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGLAUNCH,
DRUGMONOG2, KOSMET, MEDICONF, NUTRACEUT, PCTGEN, PHARMAML'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
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PROCESSING COMPLETED FOR L2
L3 43 DUP REM L2 (125 DUPLICATES REMOVED)

=> d l3 bib,kwic 1-43

L3 ANSWER 1 OF 43 TOXCENTER COPYRIGHT 2003 ACS on STN
AN 2003:204657 TOXCENTER
CP Copyright 2003 ACS
DN CA13909127982R
TI Peptides and peptidomimetics having anti-proliferative activity and/or that augment nucleic acid damaging agents or treatments
AU Kawabe, Takumi; Kobayashi, Hidetaka
CS ASSIGNEE: Canbas Research Laboratories, Ltd.
PI WO 2003059942 A2 24 Jul 2003
SO (2003) PCT Int. Appl., 75 pp.
CODEN: PIXXD2.
CY JAPAN
DT Patent
FS CAPLUS
OS CAPLUS 2003:571012
LA English
ED Entered STN: 20030819
Last Updated on STN: 20030825
RN 12587-46-1 (Alpha particle)
12587-47-2 (.beta.-Particle)
154907-65-0 (Chk1 kinase)
51-21-8 (5-Fluorouracil)
7689-03-4 (**Camptothecin**)
11056-06-7 (Bleomycin)
15663-27-1 (Cisplatin)
25316-40-9 (Adriamycin)
61825-94-3 (Oxaliplatin)
68247-85-8 (Pepleomycin)
93908-02-2 (**Rebeccamycin**)
565434-68-6 (CBP 511)
565434-72-2 (CBP 510)
565434-73-3 (CBP 512)
565434-76-6 (CBP 608)
565434-77-7 (CBP 700)
565434-79-9 (CBP 701)
565434-81-3 (CBP. . .

L3 ANSWER 2 OF 43 USPATFULL on STN
AN 2003:201367 USPATFULL
TI Compositions and methods for the treatment of inflammatory diseases
IN Jackson, John K., Vancouver, CA, UNITED STATES
Burt, Helen M., Vancouver, CANADA
Dordunoo, Stephen K., Baltimore, MD, UNITED STATES
PI US 2003139353 A1 20030724
AI US 2002-220190 A1 20021203 (10)
WO 2001-CA247 20010228
DT Utility
FS APPLICATION
LREP BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO PARK, CA, 94025
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2283
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . inhibits that may be used in this invention include topoisomerase I inhibitors and topoisomerase II inhibitors. Topoisomerase I inhibitors include **camptothecin**, indoinoquinolinediones; NS6314662; benzoanthracenes, such as

saintopinsana UC36; benzophenathidines, such as nitidine, fagaronine and coralyne, intoplicine; indolocarbazoles such as NB506, KT6006 and **rebeccamycin**; anthracyclines such as norpholinodoxorubicin, aclacinomycin and rudofomycin; peptides such as actinomycin, and NUICRF505; benzimidazoles such as Hoechst 33342 and 2,5-substituted. . .

L3 ANSWER 3 OF 43 USPATFULL on STN
AN 2003:120787 USPATFULL
TI Topoisomerase I selective cytotoxic sugar derivatives of indolopyrrolocarbazoles
IN Ruediger, Edward H., Greenfield Park, CANADA
Saulnier, Mark G., Higganum, CT, UNITED STATES
Beaulieu, Francis, Laprairie, CANADA
Bachand, Carol, Candiac, CANADA
Balusubramanian, Neelakantan, Madison, CT, UNITED STATES
Long, Byron Hepler, Doylestown, PA, UNITED STATES
Frennesson, David B., Naugatuck, CT, UNITED STATES
Zimmermann, Kurt, Durham, CT, UNITED STATES
Naidu, B. Narasimhulu, Durham, CT, UNITED STATES
Stoffan, Karen, Hartford, CT, UNITED STATES
St. Laurent, Denis Robert, Newington, CT, UNITED STATES
PI US 2003083271 A1 20030501
AI US 2002-103908 A1 20020322 (10)
PRAI US 2001-278043P 20010322 (60)
DT Utility
FS APPLICATION
LREP STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1215
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0005] A recent review highlights some of the non **camptothecin** topoisomerase I active agents (Expert Opin. Ther. Pat. 10:635-666, 2000). Further, indolo[2,3-a]carbazole derivatives related to the **Rebeccamycin** class, such as NB-506, are disclosed (EP Appl. 0 545 195 B1 and 0,602,597 A2; Cancer Research 1993, 53, 490-494; ibid 1995, 55, 1310-1315) and claimed to exhibit antitumor activity. However, unlike **camptothecin** which acts as a selective topo I poison, these derivatives have been reported to be non-selective, exhibiting additional biological effects,. . . kinase activity (Molecular Pharmacol. 1999, 56, 185-195) and topoisomerase II activity (Proc. AACR 1997, 38, 75). Indolo[2,3-a]carbazole alkaloids such as **rebeccamycin** (U.S. Pat. Nos. 4,487,925 and 4,552,842) and its water-soluble, clinically-active analog, 6-(2-diethylaminoethyl) **rebeccamycin** (U.S. Pat. No. 4,785,085), are useful antitumor agents which target DNA. Related indolocarbazoles are also disclosed (WO 9530682) and claimed. . .
SUMM [0007] More recently Prudhomme, et al. report a series of indolocarbazoles derived from **rebeccamycin** which all display a so-called resistance index below 20 (Current Medicinal Chemistry 2000, 7, 1189). The resistance index was defined. . . as IC.sub.50 P388CPT5/IC.sub.50 P388, where these IC.sub.50's are measures of the antiproliferative activities against murine P388CPT5 leukemia cells resistant to **camptothecin** and parental P388 cells, respectively.

L3 ANSWER 4 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2003-32740 DRUGU P B C
TI Structure-activity relationships of fluoroindolocarbazole-based topoisomerase I targeting agents.
AU Long B H; Balasubramanian B N; Fairchild C; Saulnier M; Ruediger E;

Zimmermann K; Naidu N; Beaulieu F; Martel A; Vyas D
CS Bristol-Squibb
LO Princeton, N.J.; Wallingford, Conn., USA; Candiac, Ont., Can.
SO Proc.Am.Assoc.Cancer Res. (94 Meet., 403, 2003) ISSN: 0197-016X
AV Bristol-Myers Squibb, Princeton, NJ, U.S.A. (11 authors).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Fluoroindolocarbazole analogs related to **rebeccamycin** were prepared and evaluated for their in-vitro capacities to induce topoisomerase (T)-I mediated single-strand breaks in DNA and for their. . . lacked functional T-I (R). Substitutions of the pendent glucose with specific sugars yielded potent compounds with IC50 values equivalent to **camptothecin**. Substitution of the 4'-OH with H or F resulted in increased potencies towards T-I and greatly increased cytotoxic potencies. SAR. . .
ABEX. . . . of the pendent glucose with specific sugars (including amino sugars) yielded potent compounds with IC50 values equivalent to that of **camptothecin**. Substitution of the 4'-OH with H or F resulted in increased potencies towards T-I and greatly increased cytotoxic potencies with IC50 values as much as 20-fold more potent than **camptothecin** for T-I-mediated DNA cleavage and cytotoxicity. (Y225)
CT [01] **REBECCAMYCIN** *RC; **CAMPTOTHECIN** *RC; EC-5.99.1.2 *FT; IN-VITRO *FT; SYNTH. *FT; STRUCT.ACT. *FT; P388-CELL *FT; CYTOSTATIC *FT; TOPOISOMERASE-I-INHIBITOR *FT; DNA-TOPOISOMERASE *FT; DNA-TOPOISOMERASE-I *FT; TISSUE-CULTURE. . .

L3 ANSWER 5 OF 43 IFIPAT COPYRIGHT 2003 IFI on STN DUPLICATE 1
AN 10091526 IFIPAT;IFIUDB;IFICDB
TI COMPOSITIONS AND METHODS FOR THE TREATMENT OF CANCER; THALIDOMIDE AND A TOPOISOMERASE INHIBITOR ANTICANCER DRUG SUCH AS IRINOTECAN; REDUCES TOXICITY RELATED SIDE EFFECTS OF ANTICANCER DRUG
INF Barer; Sol, Westfield, NJ, US
Zeitlin; Andrew L., Basking Ridge, NJ, US
Zeldis; Jerome B., Princeton, NJ, US
IN Barer Sol; Zeitlin Andrew L; Zeldis Jerome B
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG PENNIE & EDMONDS LLP, 1667 K STREET NW, SUITE 1000, WASHINGTON, DC, 20006
PI US 2002035090 A1 20020321
AI US 2001-853617 20010514
PRAI US 2000-204143P 20000515 (Provisional)
FI US 2002035090 20020321
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 60
ACLM 5. The method of claim 1 or 2 wherein the topoisomerase inhibitor is selected from the group consisting of **camptothecin**, iriniotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED-110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, IST-622, rubitecan, pyrazoloacridine, XR-5000, and pharmaceutically acceptable. . .
18. The method of claim 12 wherein the topoisomerase inhibitor is selected from the group consisting of **camptothecin**, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED- 110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . .

46. The pharmaceutical composition of claim 45 wherein the topoisomerase inhibitor is selected from the group consisting of **camptothecin**, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED-110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . .

50. The dosage form of claim 49 wherein the topoisomerase inhibitor is selected from the group consisting of **camptothecin**, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE 1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED-110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . .

58. The kit of claim 57 wherein the topoisomerase inhibitor is selected from the group consisting of **camptothecin**, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED- 110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . .

L3 ANSWER 6 OF 43 USPATFULL on STN
AN 2002:199128 USPATFULL
TI Topoisomerase inhibitors
IN Saulnier, Mark G., Higganum, CT, UNITED STATES
Ruediger, Edward H., Greenfield Park, CANADA
Balasubramanian, Neelakantan, Madison, CT, UNITED STATES
Mahler, Mikael, Outremont, CANADA
Beaulieu, Francis, Laprairie, CANADA
Bachand, Carol, Candiac, CANADA
Frennesson, David B., Naugatuck, CT, UNITED STATES
PI US 2002107237 A1 20020808
AI US 2001-965976 A1 20010927 (9)
PRAI US 2000-238726P 20001006 (60)
DT Utility
FS APPLICATION
LREP STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1234
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0005] Indolo[2,3-a]carbazole derivatives related to the **Rebeccamycin** class are disclosed (EP Appl. 0 545 195 B1 and 0,602,597 A2; Cancer Research 1993, 53, 490-494; ibid 1995, 55,. . . 1310-1315) and claimed to exhibit anti-tumor activity; however the major mechanism of action of these derivatives may not be like **camptothecin**, which acts as a topoisomerase I poison.

L3 ANSWER 7 OF 43 USPATFULL on STN
AN 2002:133847 USPATFULL
TI Tumor proliferation inhibitors
IN Ruediger, Edward H., Quebec, CANADA
Balasubramanian, Neelakantan, Madison, CT, UNITED STATES
Mahler, Mikael, Outremont, CANADA
Bachand, Carol, Candiac, CANADA
Beaulieu, Francis, Laprairie, CANADA
PI US 2002068705 A1 20020606
AI US 2001-962181 A1 20010925 (9)

PRAI US 2000-238712P 20001006 (60)
DT Utility
FS APPLICATION
LREP STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 771
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0004] Indolo[2,3-a]carbazole alkaloids such as **rebeccamycin** (U.S. Pat. No. 4,487,925 and 4,552,842) and its water-soluble, clinically-active analog, 6-(2-diethylaminoethyl)**rebeccamycin** (U.S. Pat. No. 4,785,085), are useful antitumor agents which target DNA. Furthermore, fluoroindolocarbazoles (WO 98/07433) have been disclosed as antineoplastic agents with topoisomerase I inhibitory activity. Indolo[2,3-a]carbazole derivatives related to the **Rebeccamycin** class are disclosed (EP Appl. 0 545 195 B1 and 0,602,597 A2; Cancer Research 1993, 53, 490-494; ibid, 1995, 55,. . . 1310-1315) and claimed to exhibit anti-tumor activity; however the major mechanism of action of these derivatives may not be like **camptothecin**, which acts as a topoisomerase I poison. Related indolocarbazoles are also disclosed (WO 95/30682) and claimed to exhibit anti-tumor activity.. . . certain fluororebeccamycin analogs as useful antitumor agents, along with a process for their production by fluorotryptophan analog feeding of a **rebeccamycin**-producing strain of Saccharothrix aerocolonigenes, preferably Saccharothrix aerocolonigenes C38,383-RK2 (ATCC 39243). Glicksman, et al. disclose indolocarbazole alkaloids (U.S. Pat. No, 5,468,872),. . .

L3 ANSWER 8 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 2
AN 2002:185166 BIOSIS
DN PREV200200185166
TI Active site mutations in DNA topoisomerase I distinguish the cytotoxic activities of **camptothecin** and the indolocarbazole, **rebeccamycin**.
AU Woo, Michael H.; Vance, John R.; Otero Marcos, Ana R.; Bailly, Christian; Bjornsti, Mary-Ann (1)
CS (1) Dept. Molecular Pharmacology, St. Jude Children's Research Hospital, 332 N. Lauderdale, Memphis, TN, 38105: Mary-Ann.Bjornsti@stjude.org USA
SO Journal of Biological Chemistry, (February 8, 2002) Vol. 277, No. 6, pp. 3813-3822. http://www.jbc.org/. print.
ISSN: 0021-9258.
DT Article
LA English
TI Active site mutations in DNA topoisomerase I distinguish the cytotoxic activities of **camptothecin** and the indolocarbazole, **rebeccamycin**.
AB DNA topoisomerase I (Top1p) catalyzes topological changes in DNA and is the cellular target of the antitumor agent **camptothecin** (CPT). Non-CPT drugs that target Top1p, such as indolocarbazoles, are under clinical development. However, whether the cytotoxicity of indolocarbazoles derives from Top1p poisoning remains unclear. To further investigate indolocarbazole mechanism, **rebeccamycin** R-3 activity was examined in vitro and in yeast. Using a series of Top1p mutants, where substitution of residues around. . .
IT . . .
Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology
IT Chemicals & Biochemicals
DNA topoisomerase I [Top1p]: active site mutations, catalytic activity; **camptothecin** [CPT]: antineoplastic - drug, cytotoxic activity; **rebeccamycin** R-3: antineoplastic - drug, cytotoxic activity,

indolocarbazole

L3 ANSWER 9 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2003:164415 BIOSIS
DN PREV200300164415
TI DNA binding and topoisomerase I poisoning activities of novel disaccharide indolocarbazoles.
AU Facompre, Michael; Carrasco, Carolina; Colson, Pierre; Houssier, Claude; Chisholm, John D.; Van Vranken, David L.; Bailly, Christian (1)
CS (1) INSERM U-524, Laboratoire de Pharmacologie Antitumorale, du Centre Oscar Lambret, IRCL, 59045, Cedex Lille, France: bailly@lille.inserm.fr France
SO Molecular Pharmacology, (November 2002, 2002) Vol. 62, No. 5, pp. 1215-1227. print.
ISSN: 0026-895X.
DT Article
LA English
AB The antibiotics AT2433-A1 and AT2433-B1 are two indolocarbazole diglycosides related to the antitumor drug **rebeccamycin** known to stabilize topoisomerase I-DNA complexes. This structural analogy prompted us to explore the binding of four indolocarbazole diglycosides with. . . contrast to the uncharged diglycoside JDC-277, which stimulates DNA cleavage by the enzyme mainly at TG sites, as observed with **camptothecin**. Cytotoxicity measurements with CEM and CEM/C2 human leukemia cell lines sensitive and resistant to **camptothecin**, respectively, also suggested that topoisomerase I contributes, at least partially, to the mechanism of action of the neutral diglycoside JDC-277. . .

L3 ANSWER 10 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2003-09126 DRUGU C B P
TI DNA targeting of two new antitumour rebeccamycin derivatives.
AU Facompre M; Baldeyrou B; Bailly C; Anizon F; Marminon C; Prudhomme M; Colson P; Houssier C
CS INSERM; Univ.Clermont-Ferrand-Blaise-Pascal; Univ.Liege
LO Lille; Aubiere, Fr.; Liege, Belg.
SO Eur.J.Med.Chem. (37, No. 12, 925-32, 2002) 7 Fig. 1 Tab. 20 Ref.
CODEN: EJMCA5 ISSN: 0223-5234
AV INSERM U524 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Place de Verdun, 59045 Lille, France. (C.B.). (e-mail: bailly@lille.inserm.fr).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The recently reported indolocarbazole **rebeccamycin** -staurosporine hybrids MP-003, MP-024, MP-059 and MP-072 differed in their affinity for DNA. Affinity was much higher for the cationic MP-059. . . inhibited by MP-024 but not by MP-059 or MP-072. None of the compounds inhibited human topoisomerase-II. The reference agents were **camptothecin** and etoposide (both Sigma-Chem.).
ABEX. . . MP-059 than for MP-072. A relaxation assay using supercoiled plasmid DNA showed that MP-024 (2-50 uM) inhibited topoisomerase-I activity. Like **camptothecin**, MP-024 increased enzyme-mediated DNA single-strand breaks. MP-059 and MP-072 did not interact with the enzyme. 7 Fig. 1 Tab. 20. . .

L3 ANSWER 11 OF 43 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
DUPLICATE
AN 2002:34649875 BIOTECHNO
TI Discovery of antitumor indolocarbazoles: **Rebeccamycin**, NSC 655649, and fluoroindolocarbazoles
AU Long B.H.; Rose W.C.; Vyas D.M.; Matson J.A.; Forenza S.

CS B.H. Long, Pharmaceutical Research Institute, Bristol-Myers Squibb, Princeton, NJ 08543-4000, United States.
E-mail: byron.long@bms.com
SO Current Medicinal Chemistry - Anti-Cancer Agents, (2002), 2/2 (255-266), 58 reference(s)
CODEN: CMCACI ISSN: 1568-0118
DT Journal; General Review
CY Netherlands
LA English
SL English
TI Discovery of antitumor indolocarbazoles: **Rebeccamycin**, NSC 655649, and fluoroindolocarbazoles
AB . . . anticancer drugs conducted by Bristol-Myers in the 1970s and early 1980s resulted in the identification of a novel indolocarbazole (IC) **rebeccamycin** (RBM) as a potential drug development candidate. Subsequently, an analog program designed to impart distal site in vivo antitumor activity. . . . I was confirmed by production of topo I-mediated single-strand breaks in DNA at sites essentially identical to those induced by **camptothecin**. Topo I dependent cytotoxicity was demonstrated for specific FICs using a P388 and **camptothecin** -resistant P388/CPT45 pair of cell lines, the latter expresses little or no functional topo I. For example, topo I selectivity was. . . . FIC and was least significant and least cytotoxic with 4,8-difluoro substituted FIC. The review focuses on the discovery of the **rebeccamycin** class of compounds and their structure-activity relationships leading to the development of the clinical candidate BMY-27557 (NSC 655649), as well. . . .
CT. . . . activity relation; ovary cancer; neutropenia; thrombocytopenia; dose response; drug structure; human; nonhuman; mouse; controlled study; human cell; animal cell; review; **rebeccamycin**; 1,11 dichloro 6 (2 diethylaminoethyl) 12,13 dihydro 5h indolo[2,3 a]pyrrolo[3,4 c]carbazole 5,7(6h) dione 13 (4 o methylglucoside); 1,11 deschloro 1,11. . . . bms 250749; carbazole derivative; 2 diethylaminoethanol; bmy 27557 14; DNA topoisomerase; DNA topoisomerase (ATP hydrolysing); tryptophan derivative; single stranded DNA; **camptothecin**; at2433 a1; at2433 b1; staurosporine; k 252a; k 252b; 7 oxostaurosporine; staurosporine derivative; teniposide; etoposide; doxorubicin; 6 formylamino 12,13 dihydro. . .
RN (**rebeccamycin**) 93908-02-2; (2 diethylaminoethanol) 100-37-8; (DNA topoisomerase) 80449-01-0; (**camptothecin**) 7689-03-4; (at2433 a1) 102644-20-2; (at2433 b1) 102622-96-8; (staurosporine) 62996-74-1; (k 252a) 97161-97-2; (k 252b) 99570-78-2; (teniposide) 29767-20-2; (etoposide) 33419-42-0; (doxorubicin). . .

L3 ANSWER 12 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-24968 DRUGU P
TI DNA topoisomerase I is the cellular target of the indolocarbazole rebeccamycin R-3.
AU Woo M H; Vance J R; Bailly C; Bjornsti M A
LO Memphis, Tenn., USA; Lille, Fr.
SO Proc.Am.Assoc.Cancer Res. (43, 93 Meet., 246-47, 2002) ISSN: 0197-016X
AV St. Jude Children's Research Hospital, Memphis, TN, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB In-vitro, DNA topoisomerase 1 (Top1p) acted as cellular target for **rebeccamycin** R-3. R-3 is an indolocarbazole antitumor agent. (conference abstract: 93rd Annual Meeting of the American Association for Cancer Research, San. . .
ABEX. . . Substituting His, Ser or Asp for Asn immediately N-terminal to the active site Tyr in Top1p altered enzyme function and **camptothecin** (CPT) sensitivity. Ser or Asp mutant enzyme was resistant to CPT,

whereas His mutant enzyme was hypersensitive to CPT. Like. . .

L3 ANSWER 13 OF 43 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
AN 2002:34655784 BIOTECHNO
TI Sequence-specific interactions of drugs interfering with the topoisomerase-DNA cleavage complex
AU Palumbo M.; Gatto B.; Moro S.; Sissi C.; Zagotto G.
CS M. Palumbo, Dept. of Pharmaceutical Sciences, University of Padova, Via Marzolo 5, 35131 Padua, Italy.
E-mail: manlio.palumbo@unipd.it
SO Biochimica et Biophysica Acta - Molecular Basis of Disease, (18 JUL 2002), 1587/2-3 (145-154), 76 reference(s)
CODEN: BBADEX ISSN: 0925-4439
PUI S0925443902000777
DT Journal; General Review
CY Netherlands
LA English
SL English
CT. . . DNA binding; DNA damage; catalysis; drug specificity; DNA sequence; human; nonhuman; review; priority journal; antineoplastic agent; anthracycline; mitoxantrone; amsacrine; epipodophyllotoxin; **camptothecin**; indolocarbazole; 6 [2 (dimethylamino)ethylamino] 3 hydroxy 7h indeno[2,1 c]quinolin 7 one; n (2 dimethylaminoethyl) 4 acridinecarboxamide; DNA base; isoenzyme; topotecan; irinotecan; pibenzimol; 4 [5 (4 methyl 1 piperazinyl)[2,5' bi 1h benzimidazol] 2' yl]phenol; hoe 33342; **rebeccamycin**; acridine; anthraquinone; ellipticine; bisantrene; dactinomycin; terpenoid; quinolone derivative; flavonoid; saintopin; intoplicine; aclarubicin; unindexed drug; unclassified drug; cp 115953
RN (DNA topoisomerase) 80449-01-0; (mitoxantrone) 65271-80-9, 70476-82-3; (amsacrine) 51264-14-3, 54301-15-4; (epipodophyllotoxin) 4375-07-9; (**camptothecin**) 7689-03-4; (6 [2 (dimethylamino)ethylamino] 3 hydroxy 7h indeno[2,1 c]quinolin 7 one) 174634-08-3, 174634-09-4; (n (2 dimethylaminoethyl) 4 acridinecarboxamide) 89459-25-6; (topotecan). . . 123948-87-8; (irinotecan) 100286-90-6; (pibenzimol) 23491-44-3; (4 [5 (4 methyl 1 piperazinyl)[2,5' bi 1h benzimidazol] 2' yl]phenol) 23491-45-4; (hoe 33342) 23491-52-3; (**rebeccamycin**) 93908-02-2; (acridine) 260-94-6; (anthraquinone) 84-65-1; (ellipticine) 519-23-3; (bisantrene) 71439-68-4, 78186-34-2; (dactinomycin) 1402-38-6, 1402-58-0, 50-76-0; (intoplicine) 125974-72-3; (aclarubicin) 57576-44-0, 75443-99-1
CN

L3 ANSWER 14 OF 43 TOXCENTER COPYRIGHT 2003 ACS on STN
AN 2001:219853 TOXCENTER
CP Copyright 2003 ACS
DN CA13526366733J
TI Compositions and methods for the treatment of cancer
AU Zeldis, Jerome B.; Zeitlin, Andrew; Barer, Sol
CS ASSIGNEE: Celgene Corp.
PI WO 2001087307 A2 22 Nov 2001
SO (2001) PCT Int. Appl., 44 pp.
CODEN: PIXXD2.
CY UNITED STATES
DT Patent
FS CAPLUS
OS CAPLUS 2001:850945
LA English
ED Entered STN: 20011211
Last Updated on STN: 20020326
RN 128201-92-3 (IST 622)
118736-03-1 (KT 6006)
145308-04-9 (KT 6528)
4707-32-8 (.beta.-Lapachone)
6872-57-7 (Nitidine)

6872-73-7 (Coralyne)
6873-09-2 (Epiberberine)
7689-03-4 (**Camptothecin**)
23491-45-4 (Hoechst 33258)
52259-65-1 (Fagaronine)
62417-80-5 (Bulgarein)
86639-52-3 (SN-38)
89458-99-1 (XR-5000)
91421-42-0 (Rubitecan)
91421-43-1 (9-Aminocamptothecin)
93908-02-2 (**Rebeccamycin**)
97682-44-5 (Irinotecan)
99009-20-8 (Pyrazoloacridine)
123948-87-8 (Topotecan)
131190-63-1 (Saintopin)
139112-73-5 (ED-110)
149882-10-0 (GG-211)
150829-94-0 (UCE6)
151069-12-4 (NB-506)
154163-86-7 (TAN-1518A)
154163-87-8 (TAN-1518B)

. . .

L3 ANSWER 15 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-36737 DRUGU B
TI Specific inhibition of serine- and arginine-rich splicing factors phosphorylation, spliceosome assembly, and splicing by the antitumor drug NB-506.
AU Pilch B; Allemand E; Facompre M; Bailly C; Riou J F; Soret J; Tazi J
CS CNRS; Univ.Montpellier; Univ.Reims; INSERM
LO Montpellier, Reims; Lille, Fr.
SO Cancer Res. (61, No. 18, 6876-84, 2001) 8 Fig. 39 Ref.
CODEN: CNREA8 ISSN: 0008-5472
AV IGM-CNRS, 1919 Route de Mende, 34293 Montpellier, France. (J.T.).
(e-mail: tazi@igm.cnrs-mop.fr).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB. . . treated with NB-506 failed to phosphorylate SF2/ASF and to support splicing of pre-mRNA substrates containing SF2/ASF-target sequences. NB-506, but not **rebeccamycin** and **camptothecin** (CPT), inhibited splicing. NB-506 also differentially affected the phosphorylation status of SR proteins in P388 and P388CPT5 leukemia cells resistant. . .
ABEX. . . preparation of HeLa NE was supplemented with NB-506 (25-100 uM), splicing was dose-dependently inhibited. No such inhibition was observed with **rebeccamycin** or CPT. In P388 cells, SDS-PAGE showed that at higher NB-506 concentrations, labeling of SRp20 and SRp40 was abolished and. . .
CT [01] NB-506 *PH; BANYU *FT; **REBECCAMYCIN** *RC; **CAMPTOTHECIN** *RC; DR9504338 *RN; TOPOISOMERASE-I-INHIBITOR *FT; EC-5.99.1.2 *FT; INHIBITION *FT; PHOSPHORYLATION *FT; HELA-CELL *FT; NUCLEUS *FT; P388-CELL *FT; LEUKEMIA *FT; GENE. . .

L3 ANSWER 16 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-03992 DRUGU B P
TI Fluoroindolocarbazoles, a novel topoisomerase I targeting chemotype with potential as anticancer agents.
AU Long B H; Woessner R D; Wang R R; Lam K S; Schroeder D R; Matson J A; Menzel R; Forenza S
CS Bristol-Squibb; MedImmune; Optigenix
LO Princeton, N.J., Gaithersburg, Md.; Newark, Del., USA
SO Proc.Am.Assoc.Cancer Res. (42, 92 Meet., 719, 2001) ISSN:

0197-016X
AV Bristol-Myers Squibb, Princeton, N.J., U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The topoisomerase 1 inhibitory activity of fluoroindolocarbazoles (FICZ) was studied in-vitro. **Rebeccamycin** (RBM), BMS-181176, FICZ, staurosporine and K-252a (SF-2370) were all cytotoxic but only FICZ cytotoxicity was dependent on topo 1 in P388 and **camptothecin** -resistant P388/CPT45 cells. Structure-activity relationships are discussed. FICZ with core fluorines in positions 3 and 9 were the most active. (conference. . .
ABEX FICZ induced topo 1-mediated single-strand breaks in DNA with similar potency to **camptothecin**. RBM and K-252a had 10- and 1000-fold less potency than **camptothecin**. Breaks induced by staurosporine and K-252a occurred at the same sites as those induced by **camptothecin**. Unlike **camptothecin**, staurosporine and K-252a inhibited topo-1-mediated DNA cleavage at high concentrations. Staurosporine did not induce topo-1-mediated breaks. Indolocarbazoles inhibited the catalytic. . . All the compounds were potent cytotoxic agents but only that of FICZ was dependent on topo 1 in P388 and **camptothecin**-resistant P388/CPT45 cells. Topo 1 selectivity was greatest when both core fluorines were located in the 3 and 9 positions and. . .
CT [01] **REBECCAMYCIN** *RC; STAUROSPORINE *RC; **CAMPTOTHECIN** *RC; SF-2370 *RC; DRUG-COMPARISON *FT; STRUCT.ACT. *FT; CYTOSTATIC *FT; TOPOISOMERASE-I-INHIBITOR *FT; P388-CELL *FT; IN-VITRO *FT; TOPOISOMERASE-INHIBITOR *FT; TISSUE-CULTURE *FT; LEUKEMIA. . .

L3 ANSWER 17 OF 43 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 2001:762247 SCISEARCH
GA The Genuine Article (R) Number: BS72V
TI DNA relaxation and cleavage assays to study topoisomerase I inhibitors
AU Bailly C (Reprint)
CS Ctr Oscar Lambret, IRCL, INSERM, U524, F-59045 Lille, France (Reprint); Ctr Oscar Lambret, IRCL, Lab Pharmacol Antitumorale, F-59045 Lille, France
CYA France
SO DRUG-NUCLEIC ACID INTERACTIONS, (AUG 2001) Vol. 340, pp. 610-623. Publisher: ACADEMIC PRESS INC, 525 B STREET, SUITE 1900, SAN DIEGO, CA 92101-4495 USA.
ISSN: 0076-6879.
DT General Review; Journal
LA English
REC Reference Count: 53
STP KeyWords Plus (R): RING-MODIFIED **CAMPTOTHECIN**; EUKARYOTIC TOPOISOMERASE; ANTITUMOR AGENTS; DERIVATIVES; INDOLOCARBAZOLE; BINDING; COMPLEXES; HOMOCAMPTOTHECIN; **REBECCAMYCIN**; CYTOTOXICITY

L3 ANSWER 18 OF 43 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN DUPLICATE 5
AN 2001:575907 SCISEARCH
GA The Genuine Article (R) Number: 454PQ
TI Triple helix-forming oligonucleotides conjugated to indolocarbazole poisons direct topoisomerase I-mediated DNA cleavage to a specific site
AU Arimondo P B; Bailly C (Reprint); Boutorine A S; Moreau P; Prudhomme M; Sun J S; Garestier T; Helene C
CS IRCL, INSERM, U524, Pl verdun, F-59045 Lille, France (Reprint); IRCL, INSERM, U524, F-59045 Lille, France; IRCL, Lab Pharmacol Antitumoral, Ctr Oscar Lambret, F-59045 Lille, France; Museum Natl Hist Nat, INSERM, U201, CNRS, UMR 8646, Lab Biophys, F-75231 Paris, France; Univ Blaise Pascal, CNRS, UMR 6504, SEESIB, F-63177 Clermont Ferrand, France
CYA France
SO BIOCONJUGATE CHEMISTRY, (JUL-AUG 2001) Vol. 12, No. 4, pp. 501-509. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.

ISSN: 1043-1802.
DT Article; Journal
LA English
REC Reference Count: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
STP KeyWords Plus (R): COMPOUND 6-N-FORMYLAMINO-12,13-DIHYDRO-1,11-DIHYDROXY-13-(BETA-D-GLUCOPYRANOSYL); SEQUENCE-SPECIFIC RECOGNITION; DUPLEX DNA; CROSS-LINKING; **REBECCAMYCIN**; ANTITUMOR; COMPLEXES; **CAMPTOTHECIN**; INHIBITION; COVALENT

L3 ANSWER 19 OF 43 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 6
AN 2001:829938 CAPLUS
DN 136:112106
TI Design of new anti-cancer agents based on topoisomerase poisons targeted to specific DNA sequences
AU Arimondo, P. B.; Helene, C.
CS Laboratoire de Biophysique, Museum National d'Histoire Naturelle, UMR8646 CNRS, INSERM U201, Paris, 75005, Fr.
SO Current Medicinal Chemistry: Anti-Cancer Agents (2001), 1(3), 219-235
CODEN: CMCACI; ISSN: 1568-0118
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
RE.CNT 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A review. There is considerable interest in the development of sequence-selective DNA drugs. Chem. agents able to interfere with DNA topoisomerases - essential nuclear enzymes- are widespread in nature, and some of them have outstanding therapeutic efficacy in human cancer and infectious diseases. Several classes of antineoplastic drugs, such as amsacrine, daunorubicin, etoposide (acting on type II topoisomerases), **camptothecin** and indolocarbazole derivs. of the antibiotic **rebeccamycin** (acting on type IB topoisomerases), have been shown to stimulate DNA cleavage by topoisomerases leading to cell death. However, these mols. exhibit little sequence preference. A convenient strategy to confer sequence specificity consists in the attachment of these topoisomerase poisons to sequence-specific DNA binding elements. Among sequence-specific DNA ligands, oligonucleotides can bind with high specificity of recognition to the major groove of double-helical DNA, resulting in triple helix formation. In this context, derivs. of **camptothecin**, indolocarbazole, anthracycline and acridine poisons have been covalently tethered to triple helix-forming oligonucleotides. The use of triple-helical DNA structures offers an efficient system to target topoisomerase I and II-mediated DNA cleavage to specific sequences and to increase the drug efficacy at these sites. Chem. optimization of the conjugates is essential to the efficacy of drug targeting. Consequently, the rational design of this new class of anticancer agents, conceived from topoisomerase poisons and triplex-forming oligonucleotides, may be exploited to improve the efficacy and selectivity of the DNA damage induced by topoisomerases.

L3 ANSWER 20 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 7
AN 2002:271932 BIOSIS
DN PREV200200271932
TI DNA binding properties of the indolocarbazole antitumor drug NB-506.
AU Carrasco, Carolina; Vezin, Herve; Wilson, W. David; Ren, Jinsong; Chaires, Jonathan B.; Bailly, Christian (1)
CS (1) Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret and INSERM UR-524, IRCL, F-59045, Lille: bailly@lille.inserm.fr France
SO Anti-Cancer Drug Design, (April June, 2001) Vol. 16, No. 2-3, pp. 99-107. print.
ISSN: 0266-9536.
DT Article

LA English
AB Indolocarbazoles derived from the antibiotic **rebeccamycin** represent an important group of antitumor agents. Several indolocarbazoles are currently undergoing clinical trials. These compounds inhibit topoisomerase I to produce DNA breaks that are responsible for cell death. Unlike classical topoisomerase I poisons like **camptothecin**, glycosyl indolocarbazoles can form stable complexes with DNA even in the absence of topoisomerase I. At least in part, their. . . binding to DNA is considerably less favorable than that of doxorubicin. These biophysical data help us to understand further how **rebeccamycin**-type anticancer drugs interact with DNA.

L3 ANSWER 21 OF 43 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
AN 2000:30627466 BIOTECHNO
TI Development of new antineoplastic agents with known and novel mechanisms of action
ENTWICKLUNG NEUER ANTINEOPLASTISCH WIRKSAMER SUBSTANZEN MIT BEKANNTEN UND NEUEN WIRKUNGSPRINZIPIEN
AU Lipp H.-P.
CS Dr. H.-P. Lipp, Universitatsapotheke, Rontgenweg 9, 72076 Tubingen, Germany.
SO Krankenhauspharmazie, (2000), 21/8 (396-419), 136 reference(s)
CODEN: KRANDZ ISSN: 0173-7597
DT Journal; Article
CY Germany, Federal Republic of
LA English; German
SL English
CT. . . agent; *alkylating agent; *DNA topoisomerase inhibitor; *anthracycline antibiotic agent; *folic acid antagonist; *antisense oligonucleotide; *cancer chemotherapy; antineoplastic antibiotic; temozolomide; penclomedine; **camptothecin** derivative; 9 aminocamptothecin; **rebeccamycin**; losoxantrone; methotrexate derivative; tomudex; lometrexol; fluorouracil derivative; capecitabine; 5 ethynyluracil; edelfosine; perifosine; miltefosine; Vinca alkaloid; vinflunine; angiogenesis inhibitor; fumagillol chloroacetylcarbamate;. . .
RN (temozolomide) 85622-93-1; (penclomedine) 108030-77-9; (**rebeccamycin**) 93908-02-2; (losoxantrone) 88303-60-0; (tomudex) 112887-68-0; (lometrexol) 106400-18-4, 106400-81-1, 120408-07-3, 95693-76-8; (capecitabine) 154361-50-9; (5 ethynyluracil) 59989-18-3; (edelfosine) 65492-82-2; (perifosine) 157716-52-4; (miltefosine). . .

L3 ANSWER 22 OF 43 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
AN 2000:30982795 BIOTECHNO
TI Topoisomerase I-mediated DNA damage
AU Pourquier P.; Pommier Y.
CS P. Pourquier, Lab. Molecular Pharmacology, Division of Basic Sciences, National Cancer Institute, Bethesda, MD 20892, United States.
SO Advances in Cancer Research, (2000), 80/- (189-216), 146 reference(s)
CODEN: ACRSAJ ISSN: 0065-230X
DT Journal; General Review
CY United States
LA English
SL English
CT *DNA damage; *DNA topoisomerase; ***camptothecin**; *DNA; drug targeting; protein interaction; DNA cleavage; review; priority journal; enzyme inhibitor; topotecan; 9 aminocamptothecin; irinotecan; rubitecan; 9 nitrocamtothecin; homocamptothecin; 6 formylamino 12,13 dihydro 1,11 dihydroxy 5h indolo[2,3 a][pyrrolo[3,4 c]carbazole 5,7(6h) dione 13 glucoside; intoplicine; **rebeccamycin**; ecteinascidin 743; nitidine; fagaronine; antineoplastic agent; unclassified drug; hoe 33342; dx 8951
RN (DNA topoisomerase) 80449-01-0; (**camptothecin**) 7689-03-4; (DNA) 9007-49-2; (topotecan) 119413-54-6, 123948-87-8; (irinotecan)

100286-90-6; (6 formylamino 12,13 dihydro 1,11 dihydroxy 5h indolo[2,3 a][pyrrolo[3,4 c]carbazole 5,7(6h) dione 13 glucoside) 151069-12-4; (intoplicine) 125974-72-3; (**rebeccamycin**) 93908-02-2; (ecteinascidin 743) 114899-77-3; (nitidine) 13063-04-2, 6872-57-7; (fagaronine) 52259-65-1; (hoe 33342) 23491-52-3
CN Drug Trade Name: hoechst 33342; nb 506;. . .

L3 ANSWER 23 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8
AN 2000:186458 BIOSIS
DN PREV200000186458
TI Cellular uptake and interaction with purified membranes of rebeccamycin derivatives.
AU Goossens, Jean-Francois; Henichart, Jean-Pierre; Anizon, Fabrice; Prudhomme, Michelle; Dugave, Christophe; Riou, Jean-Francois; Bailly, Christian (1)
CS (1) INSERM U-524 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Place de Verdun, 59045, Lille France
SO European Journal of Pharmacology, (Feb. 18, 2000) Vol. 389, No. 2-3, pp. 141-146.
ISSN: 0014-2999.
DT Article
LA English
SL English
AB **Rebeccamycin** is an antitumor antibiotic possessing a DNA-intercalating indolocarbazole chromophore linked to a glycosyl residue. The carbohydrate moiety of **rebeccamycin** and related synthetic analogues, such as the potent antitumor drug NB-506 (6-N-formylamino-12,13-dihydro-1,11-dihydroxy-13-(beta-D-glucopyranosyl)-5H-indolo(2,3-a)pyrrolo-(3,4-c) carbazole-5,7-(6H)-dione), is a key element for both DNA-binding and inhibition of DNA topoisomerase I. In this study, we have investigated the cellular uptake of **rebeccamycin** derivatives and their interaction with purified membranes. The transport of radiolabeled (3H)dechlorinated **rebeccamycin** was studied using the human leukemia HL60 and melanoma B16 cell lines as well as two murine leukemia cell lines sensitive (P388) or resistant (P388CPT5) to **camptothecin**. In all cases, the uptake is rapid but limited to about 6% of the drug molecules. In HL60 cells, the. . . min. The efflux of exchangeable radiolabeled molecules was relatively weak. Fluorescence studies were performed to compare the interaction of a **rebeccamycin** derivative and its aglycone with membranes purified from HL60 cells. The glycosylated drug molecules bound to the cell membranes can. . . little or no exchange upon the addition of DNA. The membrane transport and binding properties of indolocarbazole drugs related to **rebeccamycin** are reminiscent to those of other DNA-intercalating antitumor agents. The uptake most likely occurs via a passive diffusion through the. . .

L3 ANSWER 24 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 9
AN 1999:355933 BIOSIS
DN PREV199900355933
TI The **camptothecin**-resistant topoisomerase I mutant F361S is cross-resistant to antitumor **rebeccamycin** derivatives. A model for topoisomerase I inhibition by indolocarbazoles.
AU Bailly, Christian (1); Carrasco, Carolina; Hamy, Francois; Vezin, Herve; Prudhomme, Michelle; Saleem, Ahamed; Rubin, Eric
CS (1) Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, U-524 INSERM, IRCL, Place de Verdun, 59045, Lille France
SO Biochemistry, (July 6, 1999) Vol. 38, No. 27, pp. 8605-8611.
ISSN: 0006-2960.
DT Article
LA English
SL English

TI The **camptothecin**-resistant topoisomerase I mutant F361S is cross-resistant to antitumor **rebeccamycin** derivatives. A model for topoisomerase I inhibition by indolocarbazoles.

AB DNA topoisomerase I is a major cellular target for antitumor indolocarbazole derivatives (IND) such as the antibiotic **rebeccamycin** and the synthetic analogue NB-506 which is undergoing phase I clinical trials. We have investigated the mechanism of topoisomerase I inhibition by a **rebeccamycin** analogue, R-3, using the wild-type human topoisomerase I and a well-characterized recombinant enzyme, F361S. The catalytic activity of this mutant remains fully intact, but the enzyme is resistant to inhibition by **camptothecin** (CPT). Here we show that the mutated enzyme is cross-resistant to the **rebeccamycin** analogue. Despite their profound structural differences, CPT and R-3 interfere similarly with the activity of the wild-type and mutant topoisomerase. . .

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques; Pharmacology

IT Chemicals & Biochemicals
camptothecin [CPT]: Sigma Chemical Co., pharmaceutical, enzyme inhibitor, topoisomerase I inhibitor, analysis; human topoisomerase I: TopoGen Inc., inhibition, mutant, wild-type, analysis; indolocarbazoles: analysis, topoisomerase I inhibitor, enzyme inhibitor; **rebeccamycin** derivatives: analysis, pharmaceutical, antitumor antibiotic, cross-resistance; DNA-topoisomerase I covalent complex: analysis, structural elements; F361S: analysis, **camptothecin**-resistant topoisomerase I mutant; R-3: analysis, topoisomerase I inhibitor, **rebeccamycin** analogue, pharmaceutical, enzyme inhibitor

RN 7689-03-4 (**CAMPTOTHECIN**)
80449-01-0 (TOPOISOMERASE)
93908-02-2D (**REBECCAMYCIN**)
143180-75-0 (DNA-TOPOISOMERASE I)

L3 ANSWER 25 OF 43 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
AN 1999:29269119 BIOTECHNO
TI A new mechanism of acquisition of drug resistance by partial duplication of topoisomerase I
AU Komatani H.; Morita M.; Sakaizumi N.; Fukasawa K.; Yoshida E.; Okura A.; Yoshinari T.; Nishimura S.
CS H. Komatani, Banyu Tsukuba Research Institute, Merck Research Laboratories, 3 Okubo, Tsukuba-shi, Ibaraki 300-2611, Japan.
SO Cancer Research, (01 JUN 1999), 59/11 (2701-2708), 44 reference(s)
CODEN: CNREA8 ISSN: 0008-5472
DT Journal; Article
CY United States
LA English
SL English

AB. . . The indolocarbazole compound 6-N- formylamino-12,13-dihydro-1,11-dihydroxy-13-(.beta.-D-glucopyranosyl)-5H- indolo.cents.2,3-a!pyrrolo-.cents.3,4-c!carbazole-5,7(6H)-dione (NB-506) is a potent inhibitor of the religation step of topo I reaction, like **camptothecin** (CPT). We established a NB-506-resistant cell line from murine leukemia cell line P388. This resistant cell line, P388/F11, exhibited 73-fold. . .

CT *6 formylamino 12,13 dihydro 1,11 dihydroxy 5h indolo.cents.2,3 a!.cents.pyrrolo.cents.3,4 c!carbazole 5,7(6h) dione 13 glucoside; *DNA topoisomerase; ***camptothecin***; *cross resistance; *gene duplication; topotecan; **rebeccamycin**; doxorubicin; cisplatin; etoposide; irinotecan; leukemia p 388; genetic linkage; immunoblotting; northern blotting; drug sensitivity; reverse transcription polymerase chain reaction; nonhuman;. . .

RN (6 formylamino 12,13 dihydro 1,11 dihydroxy 5h indolo.cents.2,3 a!.cents.pyrrolo.cents.3,4 c!carbazole 5,7(6h) dione 13 glucoside)

151069-12-4; (DNA topoisomerase) 80449-01-0; (**camptothecin**) 7689-03-4; (topotecan) 119413-54-6, 123948-87-8; (**rebeccamycin**) 93908-02-2; (doxorubicin) 23214-92-8, 25316-40-9; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (etoposide) 33419-42-0; (irinotecan) 100286-90-6

L3 ANSWER 26 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 10
AN 1999:404029 BIOSIS
DN PREV199900404029
TI Synthesis, mode of action, and biological activities of rebeccamycin bromo derivatives.
AU Moreau, Pascale; Anizon, Fabrice; Sancelme, Martine; Prudhomme, Michelle (1); Severe, Daniele; Riou, Jean-Francois; Goossens, Jean-Francois; Henichart, Jean-Pierre; Bailly, Christian; Labourier, Emmanuel; Tazzi, Jamal; Fabbro, Doriano; Meyer, Thomas; Aubertin, A. M.
CS (1) Synthese, Electrosynthese et Etude de Systemes a Interet Biologique, UMR 6504, Universite Blaise Pascal, 63177, Aubiere France
SO Journal of Medicinal Chemistry, (May 20, 1999) Vol. 42, No. 10, pp. 1816-1822.
ISSN: 0022-2623.
DT Article
LA English
SL English
AB Bromo analogues of the natural metabolite **rebeccamycin** with and without a methyl substituent on the imide nitrogen were synthesized. The effects of the drugs on protein kinase. . . on topoisomerase I were determined. The drugs' uptake and their antiproliferative activities against P388 leukemia cells sensitive and resistant to **camptothecin**, their antimicrobial activity against a Gram-positive bacterium (B. cereus), and their anti-HIV-1 activity were measured and compared to those of. . .

L3 ANSWER 27 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 11
AN 1999:521392 BIOSIS
DN PREV199900521392
TI Targeting topoisomerase I cleavage to specific sequences of DNA by triple helix-forming oligonucleotide conjugates. A comparison between a **rebeccamycin** derivative and **camptothecin**.
AU Arimondo, Paola B.; Bailly, Christian; Boutorine, Alexandre; Sun, Jian-Sheng (1); Garestier, Therese; Helene, Claude
CS (1) Laboratoire de biophysique, UMR 8646 CNRS-Museum national d'histoire naturelle, Inserm U201, 43, rue Cuvier, 75231, Paris France
SO Comptes Rendus de l'Academie des Sciences Serie III Sciences de la Vie, (Sept., 1999) Vol. 322, No. 9, pp. 785-790.
ISSN: 0764-4469.
DT Article
LA English
SL English; French
TI Targeting topoisomerase I cleavage to specific sequences of DNA by triple helix-forming oligonucleotide conjugates. A comparison between a **rebeccamycin** derivative and **camptothecin**.
AB. . . enzyme and an important therapeutic target in cancer chemotherapy for the camptothecins as well as for indolocarbazole antibiotics such as **rebeccamycin** and its synthetic derivatives, which stabilize the cleaved DNA-topoisomerase I complex. The covalent linkage of a triple helix-forming oligonucleotide to **camptothecin** or to the indolocarbazole derivative R-6 directs DNA cleavage by topoisomerase I to specific sequences. Sequence-specific recognition of DNA is. . . double-helical DNA and positions the drug at a specific site. The efficacy of topoisomerase I-induced DNA cleavage mediated by the **rebeccamycin**-conjugate and the **camptothecin**-conjugate was compared and related to the intrinsic potency of the isolated drugs.
IT Major Concepts

Biochemistry and Molecular Biophysics; Pharmacology
IT Chemicals & Biochemicals
camptothecin; double-helical DNA; **rebeccamycin** derivative; topoisomerase I: DNA cleaving enzyme; triple helix-forming oligonucleotide conjugates

L3 ANSWER 28 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 12
AN 1999:150408 BIOSIS
DN PREV199900150408
TI Syntheses and biological activities of rebeccamycin analogues. Introduction of a halogenoacetyl substituent.
AU Moreau, Pascale; Anizon, Fabrice; Sancelme, Martine; Prudhomme, Michelle (1); Bailly, Christian; Severe, Daniele; Riou, Jean-Francois; Fabbro, Doriano; Meyer, Thomas; Aubertin, Anne-Marie
CS (1) Univ. Blaise Pascal, Synthese Electrosynthese Etude Syst. Interet Biol., UMR 6504 du CNRS, 63177 Aubiere France
SO Journal of Medicinal Chemistry, (Feb. 25, 1999) Vol. 42, No. 4, pp. 584-592.
ISSN: 0022-2623.
DT Article
LA English
AB In the course of structure-activity relationships on **rebeccamycin** analogues, a series of compounds bearing a halogenoacetyl substituent were synthesized with the expectation of increasing the interaction with DNA, possibly via covalent reaction with the double helix. Two **rebeccamycin** analogues bearing an acetyl instead of a bromoacetyl substituent were prepared to gain an insight into the role of the. . . typical topoisomerase I poisons, and they are significantly more toxic toward P388 leukemia cells than to P388/CPT5 cells resistant to **camptothecin**. The introduction of a bromo- or chloro-acetyl substituent does not affect the capacity of the drug to interfere with topoisomerase I either in vitro or in cells. One of the bromoacetyl derivatives, compound 8, is the most cytotoxic **rebeccamycin** derivative among the hundred of derivatives we have synthesized to date. In addition, we determined the antimicrobial activities against two. . .

L3 ANSWER 29 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 13
AN 1999:150254 BIOSIS
DN PREV199900150254
TI Enhanced binding to DNA and topoisomerase I inhibition by an analog of the antitumor antibiotic rebeccamycin containing an amino sugar residue.
AU Bailly, Christian (1); Qu, Xiaogang; Anizon, Fabrice; Prudhomme, Michelle; Riou, Jean-Francois; Chaires, Jonathan B.
CS (1) IRCL, U-124 Inst. National Sante Recherche Med., Place de Verdun, 59045 Lille France
SO Molecular Pharmacology, (Feb., 1999) Vol. 55, No. 2, pp. 377-385.
ISSN: 0026-895X.
DT Article
LA English
AB. . . . to a DNA-intercalating chromophore. This is the case with anthracyclines such as daunomycin and also with indolocarbazoles including the antibiotic **rebeccamycin** and its tumor active analog, NB506. In each case, the glycoside residue plays a significant role in the interaction of. . . . drug with the DNA double helix. In this study we show that the DNA-binding affinity and sequence selectivity of a **rebeccamycin** derivative can be enhanced by replacing the glucose residue with a 2'-aminoglucose moiety. The drug-DNA interactions were studied by thermal. . . . but does not appear to participate in any specific molecular contacts. The energetic contribution of the amino group of the **rebeccamycin** analog was found to be weaker than that of the sugar amino group of daunomycin, possibly because the indolocarbazole derivative. . . . the capacity of the drug to stabilize enzyme-DNA

covalent complexes. Cytotoxicity studies with P388 leukemia cells sensitive or resistant to **camptothecin** suggest that topoisomerase I represents a privileged intracellular target for the studied compounds. The role of the sugar amino group. . .

L3 ANSWER 30 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 14
AN 1999:334340 BIOSIS
DN PREV199900334340
TI Calories from carbohydrates: Energetic contribution of the carbohydrate moiety of rebeccamycin to DNA binding and the effect of its orientation on topoisomerase I inhibition.
AU Bailly, Christian (1); Qu, Xiaogang; Graves, David E.; Prudhomme, Michelle; Chaires, Jonathan B.
CS (1) Centre Oscar Lambret et INSERM U-524, Lille, 59045 France
SO Chemistry & Biology (London), (May, 1999) Vol. 6, No. 5, pp. 277-286. ISSN: 1074-5521.
DT Article
LA English
SL English
AB Background: Only a few antitumor drugs inhibit the DNA breakage-reunion reaction catalyzed by topoisomerase. One is the **camptothecin** derivative topotecan that has recently been used clinically. Others are the glycosylated antibiotic **rebeccamycin** and its synthetic analog NB-506, which is presently in phase I of clinical trials. Unlike the camptothecins, **rebeccamycin**-type compounds bind to DNA. We set out to elucidate the molecular basis of their interaction with duplex DNA, with particular. . . emphasis on the role of the carbohydrate residue. Results: We compared the DNA-binding and topoisomerase-I-inhibition activities of two isomers of **rebeccamycin** that contain a galactose residue attached to the indolocarbazole chromophore via an alpha (axial) or a beta (equatorial) glycosidic linkage.. . . Comparison with the aglycone allowed us to determine the energetic contribution of the sugar residue. Conclusions: The optimal interaction of **rebeccamycin** analogs with DNA is controlled to a large extent by the stereochemistry of the sugar residue. The results clarify the role of carbohydrates in stereospecific drug-DNA interactions and provide valuable information for the rational design of new **rebeccamycin**-type antitumor agents.

L3 ANSWER 31 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 15
AN 1999:184537 BIOSIS
DN PREV199900184537
TI Molecular basis for the stabilization of topoisomerase I-DNA covalent complexes by antitumor rebeccamycin analogs.
AU Carrasco, C. (1); Rubin, E.; Prudhomme, M.; Hamy, F.; Bailly, C.
CS (1) INSERM U-124, Lille France
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 113.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
DT Conference
LA English
IT Major Concepts
Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
camptothecin: antineoplastic - drug; **rebeccamycin**: antineoplastic - drug; sodium chloride; topoisomerase I
RN 80449-01-0 (TOPOISOMERASE)
93908-02-2 (**REBECCAMYCIN**)
7647-14-5 (SODIUM CHLORIDE)

7689-03-4 (**CAMPTOTHECIN**)

L3 ANSWER 32 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1999-32324 DRUGU P
TI Cellular uptake and membrane binding properties of an antitumor rebeccamycin derivative and its aglycone.
AU Goossens J F; Lansiaux A; Henichart J P; Riou J F; Anizon F; Prudhomme M; Bailly C
CS INSERM; Cent.Oscar-Lambret; Rhone-Poulenc-Rorer; CNRS; Univ.Clermont-Ferrand
LO Lille, Vitry sur Seine; Clermont Ferrand, Fr.
SO Proc.Am.Assoc.Cancer Res. (40, 90 Meet., 113, 1999) ISSN: 0197-016X
AV Faculte de Pharmacie, INSERM U-124 and Centre Oscar Lambret, Lille, France.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB To delineate the role of the carbohydrate moiety, the cellular uptake capacity of a **rebeccamycin** derivative and its aglycone by wild type P388 leukemia cells and 2 cell lines resistant to **camptothecin** and doxorubicin, were compared in-vitro. The study revealed that the carbohydrate domain of **rebeccamycin**-type compounds is important for the drug cellular uptake. (conference abstract: 90th Annual Meeting of the American Association for Cancer Research,. . .

L3 ANSWER 33 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 16
AN 1998:275975 BIOSIS
DN PREV199800275975
TI Syntheses and biological evaluation of indolocarbazoles, analogues of rebeccamycin, modified at the imide heterocycle.
AU Moreau, Pascale; Anizon, Fabrice; Sancelme, Martine; Prudhomme, Michelle (1); Bailly, Christian; Carrasco, Carolina; Ollier, Monique; Severe, Daniele; Riou, Jean-Francois; Fabbro, Doriano; Meyer, Thomas; Aubertin, Anne-Marie
CS (1) Synthese Etude Syst. Interet Biol., Univ. Blaise Pascal, UMR 6504 du CNRS, 63177 Aubiere France
SO Journal of Medicinal Chemistry, (May 7, 1998) Vol. 41, No. 10, pp. 1631-1640.
ISSN: 0022-2623.
DT Article
LA English
AB A series of 10 indolocarbazole derivatives, analogues to the antitumor antibiotic **rebeccamycin**, bearing modifications at the imide heterocycle were synthesized. They bear an N-methyl imide, N-methyl amide, or anhydride function instead of. . . as their antiviral activities toward HIV-1. The efficiency of the anhydride compounds was compared to that of the parent compound **rebeccamycin** and its dechlorinated analogue. All the compounds studied were inactive against PKC. The structural requirements for PKC and topoisomerase I. . . cells had little or no effect on the growth of P388CPT5 cells which are resistant to the topoisomerase I inhibitor **camptothecin**. This study reinforces the conclusion that the DNA-topoisomerase I cleavable complex is the primary cellular target of the indolocarbazoles and. . .

L3 ANSWER 34 OF 43 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
DUPLICATE
AN 1998:28446237 BIOTECHNO
TI Syntheses, biochemical and biological evaluation of staurosporine analogues from the microbial metabolite **rebeccamycin**
AU Anizon F.; Moreau P.; Sancelme M.; Voldoire A.; Prudhomme M.; Ollier M.;

Severe D.; Riou J.F.; Bailly C.; Fabbro D.; Meyer T.; Aubertin A.M.
CS M. Prudhomme, Etude de Systemes Interet Biologique, UMR 6504, Universite Blaise Pascal, 63177 Aubiere, France.
SO Bioorganic and Medicinal Chemistry, (1998), 6/9 (1597-1604), 21 reference(s)
CODEN: BMECEP ISSN: 0968-0896
PUI S0968089698000960
DT Journal; Article
CY United Kingdom
LA English
SL English
TI Syntheses, biochemical and biological evaluation of staurosporine analogues from the microbial metabolite **rebeccamycin**
AB The indolocarbazole antibiotics staurosporine and **rebeccamycin** (1) are potent antitumor drugs targeting protein kinase C and topoisomerase I, respectively. To obtain staurosporine analogues from **rebeccamycin**, different structural modifications were performed: coupling of the sugar moiety to the second indole nitrogen, dechlorination and then reduction of. . . C. Their antiproliferative effects in vitro against B16 melanoma and P388 leukemia (including the related P388CPT cell line resistant to **camptothecin**) as well as their anti-HIV-1 and antimicrobial activities against various strains of microorganisms were determined. The cytotoxicity of the dechlorinated. . .
CT *antineoplastic antibiotic; *drug synthesis; **rebeccamycin**; staurosporine; **camptothecin**; dna topoisomerase; protein kinase c; staurosporine derivative; drug activity; chemical modification; leukemia p 388; melanoma b16; cytotoxicity; antineoplastic activity; antimicrobial. . .
RN (**rebeccamycin**) 93908-02-2; (staurosporine) 62996-74-1; (**camptothecin**) 7689-03-4; (DNA topoisomerase) 80449-01-0; (protein kinase c) 141436-78-4

L3 ANSWER 35 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1998-26549 DRUGU P B
TI Diversity of DNA topoisomerases I and inhibitors.
AU Pommier Y
CS Nat.Cancer-Inst.Bethesda
LO Bethesda, Md., USA
SO Biochimie (80, No. 3, 255-70, 1998) 7 Fig. 200 Ref.
CODEN: BICMBE ISSN: 0300-9084
AV Laboratory of Molecular Pharmacology, Division of Basic Sciences, National Cancer Institute, Bldg. 37, Rm 5D02, Bethesda, MD 20892-4255, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB. . . I DNA topoisomerases found in eukaryotic cells and the topoisomerase I inhibited identified to date are reviewed. Drugs mentioned include **camptothecin** (CPT) and its derivatives, the benzoanthracenes, other heterocyclic aromatics such as intoplicine, azaIQD, wakayin and NSC-314622, the indolocarbazoles such as NB-506, ED-110, BE-13793C, **rebeccamycin**, KT-6006, K-252a and staurosporine, the benzimidazoles such as HOE-33342 and pibenzimol and other drugs which interact with the DNA minor. . .
ABEX. . . saintopin-E, UCE-1022, UCE-6, nitidine, fagaronine, O-methyl-fagaronine, fagaridine, isofagaridine, chelerythrine, coralyne, 5,6-dihydrocoralyne, intoplicine, wakayin and NSC-314622; the indolcarbazoles NB-506, ED-110, BE-13793C, **rebeccamycin**, KT-6006, KT-6528, K-252a and staurosporine; the benzimidazoles such as HOE-33342 and 33258; the anthracyclines such as NSC-354646, cynamomorpholino doxorubicin, doxorubicin,. . .
CT [02] **CAMPTOTHECIN** *PH; INTOPLICINE *PH; WAKAYIN *PH; NSC-314622

*PH; NB-506 *PH; ED-110 *PH; BE-13793C *PH; **REBECCAMYCIN** *PH; KT-6006 *PH; K-252A *PH; STAUROSPORINE *PH; HOE-33342 *PH; PIBENZIMOL *PH; PH *FT
[03] SN-38 *PH; AMINOCAMPTOTHECIN-9 *PH; CAMPTOTHECIN *RC;. . .

L3 ANSWER 36 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 18
AN 1997:216118 BIOSIS
DN PREV199799522622
TI DNA cleavage by topoisomerase I in the presence of indolocarbazole derivatives of rebeccamycin.
AU Bailly, Christian (1); Riou, Jean-Francois; Colson, Pierre; Houssier, Claude; Rodrigues-Pereira, Elisabete; Prudhomme, Michelle
CS (1) INSERM U124, Lab. Pharmacologie Moleculaire Antitumorale, Centre Oscar Lambret, Inst. Rech. Cancer, Place de Verdun, 59045 Lille France
SO Biochemistry, (1997) Vol. 36, No. 13, pp. 3917-3929.
ISSN: 0006-2960.
DT Article
LA English
AB. . . by indolocarbazoles, we have studied the induction of DNA cleavage by purified mammalian topoisomerase I mediated by the antitumor antibiotic **rebeccamycin** and a series of 20 indolocarbazole derivatives. The compounds tested bear (i) various functional groups on the non-indolic moiety (X. . . on the maleimido function (R-1 = H, OH, NH-2, NHCHO). Half of the ligands have the same carbohydrate moiety as **rebeccamycin** whereas the other ligands have no sugar residue. The inhibitory potency of the test compounds was assessed in vitro by. . . of the base preferences around topoisomerase I cleavage sites in various restriction fragments indicated that, in a manner similar to **camptothecin**, the **rebeccamycin** analogue R-3 stabilized topoisomerase I preferentially at sites having a T and a G on the 5' and 3' sides of the cleaved bond, respectively. By analogy with models previously proposed for **camptothecin** and numerous topoisomerase II inhibitors which intercalate into DNA, a stacking model for the interaction between DNA, topoisomerase I and. . .

L3 ANSWER 37 OF 43 CANCERLIT on STN
AN 97620937 CANCERLIT
DN 97620937
TI The cytotoxic mechanism of NB-506 involves action on both topoisomerase I and topoisomerase II (Meeting abstract).
AU Long B H; Fairchild C A; Bifano M; Kramer R
CS Oncology Drug Discovery, Bristol-Myers Squibb, PRI, Princeton, NJ 08540.
SO Proc Annu Meet Am Assoc Cancer Res, (1997) 38 A508.
ISSN: 0197-016X.
DT (MEETING ABSTRACTS)
LA English
FS Institute for Cell and Developmental Biology
EM 199710
ED Entered STN: 19980417
Last Updated on STN: 19980417
AB NB-506, an indolocarbazole structurally related to **rebeccamycin**, has been shown to be a potent inducer of topoisomerase (topo) I mediated DNA breaks in vitro and in cells,. . . though it is a DNA intercalator (Cancer Res; 55:1310 1995). Furthermore, cells selected for resistance to NB-506 are cross-resistant to **camptothecin** (camp) and have reduced topo I levels and activities (Cancer Res; 55:2806 1995), thus confirming topo I as the putative. . .

L3 ANSWER 38 OF 43 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN
AN 1995:25086201 BIOTECHNO
TI Novel indolocarbazole compound 6-N-formylamino-12,13-dihydro-1,11-dihydroxy-13-(.beta.-D-glucopyranosyl)-5H-indolo.cents.2,3-a!pyrrolo-.cents.3,4-c!carbazole- 5,7(6H)-dione (NB-506): Its potent antitumor

activities in mice
AU Arakawa H.; Iguchi T.; Morita M.; Yoshinari T.; Kojiri K.; Suda H.; Okura A.; Nishimura S.
CS Merck Research Laboratories, Banyu Tsukuba Research Institute, Okubo 3,Tsukuba 300-33, Japan.
SO Cancer Research, (1995), 55/6 (1316-1320)
CODEN: CNREA8 ISSN: 0008-5472
DT Journal; Article
CY United States
LA English
SL English
CT . . a!pyrrolo.cents.3,4 c!carbazole 5,7(6h) dione 13 glucoside; 6 formylamino 12,13 dihydro 1,11 dihydroxy 5h indolo.cents.2,3 a!pyrrolo.cents.3,4 c!carbazole 5,7(6h) dione 13 glucoside; **camptothecin**; cisplatin; dna directed dna polymerase alpha; dna topoisomerase (atp hydrolysing); dna topoisomerase inhibitor; doxorubicin; etoposide; irinotecan; k 252a; 6 formylamino 12,13 dihydro 1,11 dihydroxy 5h indolo.cents.2,3 a!.cents.pyrrolo.cents.3,4 c!carbazole 5,7(6h) dione 13 glucoside; **rebeccamycin**; rna polymerase ii; staurosporine; taxol; be 13793c; ed 110; unclassified drug; animal model; animal tissue; antineoplastic activity; article; cancer cell. . .
RN (DNA topoisomerase) 80449-01-0; (**camptothecin**) 7689-03-4; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (doxorubicin) 23214-92-8, 25316-40-9; (etoposide) 33419-42-0; (irinotecan) 100286-90-6; (k 252a) 97161-97-2; (6 formylamino 12,13 dihydro 1,11 dihydroxy 5h indolo.cents.2,3 a!.cents.pyrrolo.cents.3,4 c!carbazole 5,7(6h) dione 13 glucoside) 151069-12-4; (**rebeccamycin**) 93908-02-2; (staurosporine) 62996-74-1; (taxol) 33069-62-4
CN Drug Trade Name: adriamycin; cpt 11; k 252a; nb 506; be 13793c; ed 110

L3 ANSWER 39 OF 43 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 93:344114 SCISEARCH
GA The Genuine Article (R) Number: LD566
TI ED-110, A NOVEL INDOLOCARBAZOLE, PREVENTS THE GROWTH OF EXPERIMENTAL-TUMORS IN MICE
AU ARAKAWA H; IGUCHI T; YOSHINARI T; KOJIRI K; SUDA H; OKURA A (Reprint)
CS MERCK RES LABS, BANYU TSUKUBA RES INST, OKUBO 3, TSUKUBA 30033, JAPAN
CYA JAPAN
SO JAPANESE JOURNAL OF CANCER RESEARCH, (MAY 1993) Vol. 84, No. 5, pp. 574-581.
ISSN: 0910-5050.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
STP KeyWords Plus (R): DNA TOPOISOMERASE-II; RAT-KIDNEY CELLS; BIOLOGICAL-ACTIVITY; ANTITUMOR-ACTIVITY; POTENT INHIBITOR; PROTEIN-KINASE; PROLIFERATION; **CAMPTOTHECIN**; **REBECCAMYCIN**; REPLICATION

L3 ANSWER 40 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 19
AN 1993-08143 DRUGU B P
TI Induction of Mammalian DNA Topoisomerase I Mediated DNA Cleavage by Antitumor Indolocarbazole Derivatives.
AU Yamashita Y; Fujii N; Murakata C; Ashizawa T; Okabe M; Nakano H
CS Kyowa-Hakko
LO Tokyo, Shizuoka, Japan
SO Biochemistry (31, No. 48, 12069-75, 1992) 7 Fig. 37 Ref.
CODEN: BICHAW ISSN: 0006-2960
AV Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., 3-6-6 Asahimachi, Machida, Tokyo 194, Japan.
LA English
DT Journal

FA AB; LA; CT; MPC
FS Literature
AB. . . K-252A (SF-2370), KT-6006 and KT-6528, induced topoisomerase-I (TI) mediated DNA cleavage in vitro in a similar manner to that with **camptothecin** (CT). TI-II-mediated DNA cleavage was not induced by indolocarbazole compounds. KT-6006 induced TI-I-mediated cleavage dose-dependently, whereas KT-6528-induced cleavage was suppressed at high drug concentration. **Rebeccamycin** (RM; Bristol) was a weak inducer of TI-I-mediated DNA cleavage. Heat treatment reversed TI-I-mediated DNA cleavage by both KT-6006 and. . .
CT AMSACRINE *RC; **REBECCAMYCIN** *RC; **CAMPTOTHECIN** *RC; EC-5.99.1.2 *FT; IN-VITRO *FT; CATTLE *FT; YOUNG *FT; THYMUS *FT; INDUCTION *FT; CLEAVAGE *FT; INHIBITION *FT; DNA *FT; INTERCALATION. . .
CT AMSACRINE *RC; **REBECCAMYCIN** *RC; **CAMPTOTHECIN** *RC; EC-5.99.1.2 *FT; IN-VITRO *FT; CATTLE *FT; YOUNG *FT; THYMUS *FT; INDUCTION *FT; CLEAVAGE *FT; INHIBITION *FT; DNA *FT; INTERCALATION. . .

L3 ANSWER 41 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1988:344448 BIOSIS
DN BR35:39290
TI IDENTIFICATION AND CHARACTERIZATION OF NOVEL TOPOISOMERASE INHIBITORS.
AU LONG B H; JIMENEZ N E; MUSIAL S T; CASAZZA A M
CS CANCER RES., PHARMACEUTICAL RES. AND DEV., BRISTOL-MEYERS, WALLINGFORD, CONN. 06492.
SO 79TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW ORLEANS, LOUISIANA, USA, MAY 25-28, 1988. PROC AM ASSOC CANCER RES ANNU MEET. (1988) 29 (0), 270.
CODEN: PAMREA.
DT Conference
FS BR; OLD
LA English
IT Miscellaneous Descriptors
ABSTRACT HUMAN A549 LUNG ADENOCARCINOMA CELLS GILVOCARCIN V VIRENOMYCIN V VIRENOMYCIN M ELSAMICIN **REBECCAMYCIN CAMPTOTHECIN** CHARTREUSIN TENIPOSIDE DOXORUBICIN ANTINEOPLASTIC-DRUG DNA BREAKAGE
RN 6377-18-0 (CHARTREUSIN)
7689-03-4 (**CAMPTOTHECIN**)
23214-92-8 (DOXORUBICIN)
29767-20-2 (TENIPOSIDE)
77879-90-4 (GILVOCARCIN V)
80449-01-0 (TOPOISOMERASE)
83138-95-8 (VIRENOMYCIN V)
83138-96-9 (VIRENOMYCIN M)
93908-02-2 (**REBECCAMYCIN**)

L3 ANSWER 42 OF 43 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1986-51807 DRUGU P B
TI Kinetics of Topoisomerase Inhibition by VP16-213, VM26, Camptothecin, and Other Agents.
AU Long B H
LO Houston, Texas, United States
SO Proc.Am.Assoc.Cancer Res. (27, 77 Meet., 249, 1986) ISSN: 0197-016X
AV Bristol-Baylor Laboratory, Pharmacology Dept., Baylor College of Medicine, Houston, TX 77030, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The kinetics of topoisomerase (II) inhibition by etoposide (VP-16-213), teniposide (VM26), **camptothecin**, novobiocin, bleomycin, talisomycin gamma radiation and **rebeccamycin** was studied in

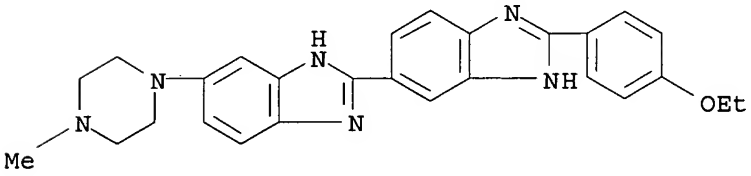
human lung adenocarcinoma cells (A549). Results indicate that the insertion of the 2 subunits of topoisomerase II. . .

ABEX. . . (SSBs) by an entirely different mechanism, also produce similar biphasic elution curves and DNA in the lysis fractions. Gamma radiation, **rebeccamycin**, and **camptothecin**, agents that produce almost no detectable DSBs, produce linear elution curves and no increase in DNA in the lysis fractions,. . .

L3 ANSWER 43 OF 43 TOXCENTER COPYRIGHT 2003 ACS on STN
AN 2002:546164 TOXCENTER
DN CRISP-97-SC06321-17
TI CHEMICAL MODIFICATION OF THE RADIATION RESPONSE
AU COOK J A
CS NCI, NIH
CSS U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NATIONAL CANCER INSTITUTE
SO Crisp Data Base National Institutes Of Health.
DT (Research)
FS CRISP
LA English
ED Entered STN: 20021200
Last Updated on STN: 20021200

AB. . . to clinicians designing human clinical trials combining paclitaxel and hyperthermia. We have also initiated studies evaluating gemcitabine, quinocarmycin, and 9-amino **camptothecin** as radiation sensitizers. Preliminary studies show that gemcitabine and 9-amino **camptothecin** enhance radiation sensitivity (enhancement ratios ranging from 1.3-1.5) of human pancreas and lung cancer cell lines. Other chemotherapy agents to be evaluated as radiation sensitizers include flavopiridol, **rebeccamycin**, and rhizoxin.

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 23491-52-3 REGISTRY
CN 2,5'-Bi-1H-benzimidazole, 2'-(4-ethoxyphenyl)-5-(4-methyl-1-piperazinyl)-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,5'-Bibenzimidazole, 2'-(p-ethoxyphenyl)-5-(4-methyl-1-piperazinyl)-
(8CI)
OTHER NAMES:
CN 2-[2-(4-Ethoxyphenyl)-6-benzimidazolyl]-6-(1-methyl-4-
piperazinyl)benzimidazole
CN Bisbenzimide
CN Ho 342
CN HOE 33342
CN **Hoechst 33342**
CN NSC 334072
FS 3D CONCORD
MF C27 H28 N6 O
CI COM
LC STN Files: ADISINSIGHT, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, DDFU,
DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, RTECS*,
TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

365 REFERENCES IN FILE CA (1907 TO DATE)
16 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
366 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

L3 ANSWER 1 OF 29 ADISCTI COPYRIGHT (C) 2003 Adis Data Information BV on STN
AN 2000:1573 ADISCTI
DN 800802887
TI The activity and pharmacokinetics of rebeccamycin analog (NSC 655649) in cancer of the biliary tract during a phase I trial.
AU Dowlati A; Majka S; Hoppel C; Ingalls S; Spiro T; et al.
SO Clinical Cancer Research (**Nov 1, 1999**), Vol. 5 (Suppl.), pp. 3729
DT Citation
RE Cancer Chemotherapy
FS Citation
LA English
PD **19991101**
CT Drug Descriptors: **Rebeccamycin**, pharmacodynamics; Antineoplastics, pharmacodynamics; Cytostatic antibiotics, pharmacodynamics; Cytostatics, pharmacodynamics; DNA antagonists, pharmacodynamics; DNA synthesis inhibitors, pharmacodynamics; DNA **topoisomerase** inhibitors, pharmacodynamics; Enzyme inhibitors, pharmacodynamics; Pre y2k drug class update, pharmacodynamics; Research drug, pharmacodynamics; **Rebeccamycin**, pharmacokinetics
CT Disease Descriptors: Cancer; Tumours
CT Other Descriptors: Research and development

L3 ANSWER 2 OF 29 ADISCTI COPYRIGHT (C) 2003 Adis Data Information BV on STN
AN 1989:5579 ADISCTI
DN 800562120
TI Novel fermentation derived cytotoxic antitumor agents.
AU Casazza A M; Schurig J E; Forenza S; et al.
SO Investigational New Drugs (**Nov 1, 1989**), Vol. 7, pp. 352
DT Citation
RE Cancer Chemotherapy
FS Citation
LA English
PD **19891101**
CT. . . Descriptors: Esperamicin A1, pharmacodynamics; Antineoplastics, pharmacodynamics; Cytostatic antibiotics, pharmacodynamics; Cytostatics, pharmacodynamics; Pre y2k drug class update, pharmacodynamics; Research drug, pharmacodynamics; **Rebeccamycin**, pharmacodynamics; DNA antagonists, pharmacodynamics; DNA synthesis inhibitors, pharmacodynamics; DNA **topoisomerase** inhibitors, pharmacodynamics; Enzyme inhibitors, pharmacodynamics
CT Disease Descriptors: Cancer; Tumours
CT Other Descriptors: Research and development

L3 ANSWER 3 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:228158 BIOSIS
DN PREV200100228158
TI Recent developments of **rebeccamycin** analogues as **topoisomerase** I inhibitors and antitumor agents.
AU Prudhomme, Michelle (1)
CS (1) Laboratoire de Synthese, Electrosynthese et Etude de Systemes a Interet Biologique, Universite Blaise Pascal, UMR 6504 du CNRS, 63177, Aubiere: mprud@chimtp.univ-bpclermont.fr France
SO Current Medicinal Chemistry, (**December, 2000**) Vol. 7, No. 12, pp. 1189-1212. print.
ISSN: 0929-8673.
DT General Review
LA English
SL English
TI Recent developments of **rebeccamycin** analogues as **topoisomerase** I inhibitors and antitumor agents.
SO Current Medicinal Chemistry, (**December, 2000**) Vol. 7, No. 12,

pp. 1189-1212. print.
ISSN: 0929-8673.
IT Major Concepts
Pharmacology; Tumor Biology
IT Diseases
cancer: neoplastic disease, treatment
IT Chemicals & Biochemicals
rebeccamycin: analogs, antitumor agent, bacterial metabolite, semi-synthetic derivatives, synthetic derivatives, **topoisomerase** I inhibitor
IT Alternate Indexing
Neoplasms (MeSH)

L3 ANSWER 4 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:231782 BIOSIS
DN PREV200000231782
TI A DNA binding indolocarbazole disaccharide derivative remains highly cytotoxic without inhibiting topoisomerase I.
AU Qu, Xiaogang; Chaires, Jonathan B.; Ohkubo, Mitsuru; Yoshinari, Tomoko; Nishimura, Susumu; Bailly, Christian (1)
CS (1) Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret and INSERM U-524, IRCL, Place de Verdun, F-59045, Lille France
SO Anti-Cancer Drug Design, (**Oct., 1999**) Vol. 14, No. 5, pp. 433-442.
ISSN: 0266-9536.
DT Article
LA English
SL English
SO Anti-Cancer Drug Design, (**Oct., 1999**) Vol. 14, No. 5, pp. 433-442.
ISSN: 0266-9536.
AB NB-506 is a glucosylated indolocarbazole related to the antibiotic **rebeccamycin** and is currently under clinical trials as an anticancer drug. This compound is a DNA intercalating agent and a potent **topoisomerase** I poison. The glucose residue attached to the planar indolocarbazole chromophore plays a significant role in the interaction of the drug with nucleic acids and contributes positively to the stabilization of **topoisomerase** I-DNA covalent complexes. To investigate further the influence of the carbohydrate moiety, we studied the DNA binding and **topoisomerase** I inhibition properties of an analogue of NB-506 bearing a disaccharide side chain. Fluorescence and footprinting studies indicate that the. . . the second sugar residue does not reinforce the interaction with DNA but abolishes the capacity of the drug to inhibit **topoisomerase** I. Unexpectedly, the disaccharide analogue of NB-506 has totally lost its capacity to stimulate DNA cleavage by **topoisomerase** I. In addition, like NB-506, the new analogue is not an inhibitor of **topoisomerase** II. However, despite the absence of **topoisomerase** poisoning activity, the cytotoxic activity is fully maintained. The maltosyl-indolocarbazole drug proved to be as potent as NB-506 at inhibiting the growth of various human and murine tumour cell lines. The study raises the question as to whether **topoisomerase** I poisoning is important for the antitumour activity of rebecca-mycin analogues.
IT . . .
IT Chemicals & Biochemicals
DNA: binding; NB-506: DNA intercalating agent, antineoplastic - drug, cytotoxicity, enzyme poison, glucose chain, glucosylated indolocarbazole, **rebeccamycin** analogue; **rebeccamycin** : pharmacodynamics; **topoisomerase** I

L3 ANSWER 5 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:186458 BIOSIS
DN PREV200000186458
TI Cellular uptake and interaction with purified membranes of rebeccamycin

derivatives.
AU Goossens, Jean-Francois; Henichart, Jean-Pierre; Anizon, Fabrice; Prudhomme, Michelle; Dugave, Christophe; Riou, Jean-Francois; Bailly, Christian (1)
CS (1) INSERM U-524 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Place de Verdun, 59045, Lille France
SO European Journal of Pharmacology, (**Feb. 18, 2000**) Vol. 389, No. 2-3, pp. 141-146.
ISSN: 0014-2999.
DT Article
LA English
SL English
SO European Journal of Pharmacology, (**Feb. 18, 2000**) Vol. 389, No. 2-3, pp. 141-146.
ISSN: 0014-2999.
AB **Rebeccamycin** is an antitumor antibiotic possessing a DNA-intercalating indolocarbazole chromophore linked to a glycosyl residue. The carbohydrate moiety of **rebeccamycin** and related synthetic analogues, such as the potent antitumor drug NB-506 (6-N-formylamino-12,13-dihydro-1,11-dihydroxy-13-(beta-D-glucopyranosyl)-5H-indolo(2,3-a)pyrrolo-(3,4-c) carbazole-5,7-(6H)-dione), is a key element for both DNA-binding and inhibition of DNA **topoisomerase** I. In this study, we have investigated the cellular uptake of **rebeccamycin** derivatives and their interaction with purified membranes. The transport of radiolabeled (3H)dechlorinated **rebeccamycin** was studied using the human leukemia HL60 and melanoma B16 cell lines as well as two murine leukemia cell lines. . . min. The efflux of exchangeable radiolabeled molecules was relatively weak. Fluorescence studies were performed to compare the interaction of a **rebeccamycin** derivative and its aglycone with membranes purified from HL60 cells. The glycosylated drug molecules bound to the cell membranes can. . . little or no exchange upon the addition of DNA. The membrane transport and binding properties of indolocarbazole drugs related to **rebeccamycin** are reminiscent to those of other DNA-intercalating antitumor agents. The uptake most likely occurs via a passive diffusion through the. . .

L3 ANSWER 6 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:538763 BIOSIS
DN PREV199900538763
TI Topoisomerase I-targetted indolocarbazole antitumor agents: Chemistry to chemotherapy.
AU Bailly, Christian (1)
CS (1) Laboratory of Antitumour Pharmacology, Unit 524 INERM Place de Verdum, Centre Oscar Lambre, Lille, 59045 France
SO Journal of Pharmacy and Pharmacology, (**Sept., 1999**) Vol. 51, No. SUPPL., pp. 112.
Meeting Info.: 136th British Pharmaceutical Conference Cardiff, Wales, UK September 13-16, 1999
ISSN: 0022-3573.
DT Conference
LA English
SO Journal of Pharmacy and Pharmacology, (**Sept., 1999**) Vol. 51, No. SUPPL., pp. 112.
Meeting Info.: 136th British Pharmaceutical Conference Cardiff, Wales, UK September 13-16, 1999
ISSN:. . .
IT . . .
digestive system disease, neoplastic disease; ovarian cancer: neoplastic disease, reproductive system disease/female
IT Chemicals & Biochemicals
irinotecan: antineoplastic - drug; **rebeccamycin**: antibiotic, antineoplastic - drug; **topoisomerase** I; topotecan: antineoplastic - drug; DNA; NB-506: antibiotic, antineoplastic - drug

IT Alternate Indexing
Colorectal Neoplasms (MeSH); Ovarian Neoplasms (MeSH)

L3 ANSWER 7 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:521392 BIOSIS
DN PREV199900521392
TI Targeting **topoisomerase** I cleavage to specific sequences of DNA by triple helix-forming oligonucleotide conjugates. A comparison between a **rebeccamycin** derivative and camptothecin.
AU Arimondo, Paola B.; Bailly, Christian; Boutorine, Alexandre; Sun, Jian-Sheng (1); Garestier, Therese; Helene, Claude
CS (1) Laboratoire de biophysique, UMR 8646 CNRS-Museum national d'histoire naturelle, Inserm U201, 43, rue Cuvier, 75231, Paris France
SO Comptes Rendus de l'Academie des Sciences Serie III Sciences de la Vie, (**Sept., 1999**) Vol. 322, No. 9, pp. 785-790.
ISSN: 0764-4469.
DT Article
LA English
SL English; French
TI Targeting **topoisomerase** I cleavage to specific sequences of DNA by triple helix-forming oligonucleotide conjugates. A comparison between a **rebeccamycin** derivative and camptothecin.
SO Comptes Rendus de l'Academie des Sciences Serie III Sciences de la Vie, (**Sept., 1999**) Vol. 322, No. 9, pp. 785-790.
ISSN: 0764-4469.
AB **Topoisomerase** I is an ubiquitous DNA cleaving enzyme and an important therapeutic target in cancer chemotherapy for the camptothecins as well as for indolocarbazole antibiotics such as **rebeccamycin** and its synthetic derivatives, which stabilize the cleaved DNA-**topoisomerase** I complex. The covalent linkage of a triple helix-forming oligonucleotide to camptothecin or to the indolocarbazole derivative R-6 directs DNA cleavage by **topoisomerase** I to specific sequences. Sequence-specific recognition of DNA is achieved by the triple helix-forming oligonucleotide, which binds to the major groove of double-helical DNA and positions the drug at a specific site. The efficacy of **topoisomerase** I-induced DNA cleavage mediated by the **rebeccamycin**-conjugate and the camptothecin-conjugate was compared and related to the intrinsic potency of the isolated drugs.
IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology
IT Chemicals & Biochemicals
camptothecin; double-helical DNA; **rebeccamycin** derivative; **topoisomerase** I: DNA cleaving enzyme; triple helix-forming oligonucleotide conjugates

L3 ANSWER 8 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:404029 BIOSIS
DN PREV199900404029
TI Synthesis, mode of action, and biological activities of rebeccamycin bromo derivatives.
AU Moreau, Pascale; Anizon, Fabrice; Sancelme, Martine; Prudhomme, Michelle (1); Severe, Daniele; Riou, Jean-Francois; Goossens, Jean-Francois; Henichart, Jean-Pierre; Bailly, Christian; Labourier, Emmanuel; Tazzi, Jamal; Fabbro, Doriano; Meyer, Thomas; Aubertin, A. M.
CS (1) Synthese, Electrosynthese et Etude de Systemes a Interet Biologique, UMR 6504, Universite Blaise Pascal, 63177, Aubiere France
SO Journal of Medicinal Chemistry, (**May 20, 1999**) Vol. 42, No. 10, pp. 1816-1822.
ISSN: 0022-2623.
DT Article
LA English
SL English
SO Journal of Medicinal Chemistry, (**May 20, 1999**) Vol. 42, No. 10, pp. 1816-1822.

ISSN: 0022-2623.

AB Bromo analogues of the natural metabolite **rebeccamycin** with and without a methyl substituent on the imide nitrogen were synthesized. The effects of the drugs on protein kinase C, the binding to DNA, and the effect on **topoisomerase** I were determined. The drugs' uptake and their antiproliferative activities against P388 leukemia cells sensitive and resistant to camptothecin, their. . . were measured and compared to those of the chlorinated and dechlorinated analogues. Dibrominated imide 5 shows a remarkable activity against **topoisomerase** I, affecting both the kinase and DNA cleavage activity of the enzyme. The marked cytotoxic potency of this compound depends essentially on its capacity to inhibit **topoisomerase** I.

IT Major Concepts
Methods and Techniques; Pharmacology

IT Chemicals & Biochemicals
rebeccamycin bromo derivatives: activity, antimitotic - drug, enzyme inhibitor - drug, synthesis, **topoisomerase** I inhibitors

L3 ANSWER 9 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:355933 BIOSIS
DN PREV199900355933
TI The camptothecin-resistant **topoisomerase** I mutant F361S is cross-resistant to antitumor **rebeccamycin** derivatives. A model for **topoisomerase** I inhibition by indolocarbazoles.
AU Bailly, Christian (1); Carrasco, Carolina; Hamy, Francois; Vezin, Herve; Prudhomme, Michelle; Saleem, Ahamed; Rubin, Eric
CS (1) Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, U-524 INSERM, IRCL, Place de Verdun, 59045, Lille France
SO Biochemistry, (**July 6, 1999**) Vol. 38, No. 27, pp. 8605-8611.
ISSN: 0006-2960.
DT Article
LA English
SL English
TI The camptothecin-resistant **topoisomerase** I mutant F361S is cross-resistant to antitumor **rebeccamycin** derivatives. A model for **topoisomerase** I inhibition by indolocarbazoles.
SO Biochemistry, (**July 6, 1999**) Vol. 38, No. 27, pp. 8605-8611.
ISSN: 0006-2960.
AB DNA **topoisomerase** I is a major cellular target for antitumor indolocarbazole derivatives (IND) such as the antibiotic **rebeccamycin** and the synthetic analogue NB-506 which is undergoing phase I clinical trials. We have investigated the mechanism of **topoisomerase** I inhibition by a **rebeccamycin** analogue, R-3, using the wild-type human **topoisomerase** I and a well-characterized recombinant enzyme, F361S. The catalytic activity of this mutant remains fully intact, but the enzyme is resistant to inhibition by camptothecin (CPT). Here we show that the mutated enzyme is cross-resistant to the **rebeccamycin** analogue. Despite their profound structural differences, CPT and R-3 interfere similarly with the activity of the wild-type and mutant **topoisomerase** I enzymes, and the drug-induced cleavable complexes are equally sensitive to the NaCl concentration. CPT and IND likely recognize identical structural elements of the **topoisomerase** I-DNA covalent complex; however, differences do exist in terms of sequence-specificity of **topoisomerase** I-mediated DNA cleavage. For the first time, a molecular model showing that CPT and IND share common steric and electronic features is proposed. The model helps to identify a specific pharmacophore for **topoisomerase** I inhibitors.

IT . . .
(Biochemistry and Molecular Biophysics); Methods and Techniques; Pharmacology

IT Chemicals & Biochemicals
camptothecin [CPT]: Sigma Chemical Co., pharmaceutical, enzyme

inhibitor, **topoisomerase** I inhibitor, analysis; human **topoisomerase** I: TopoGen Inc., inhibition, mutant, wild-type, analysis; indolocarbazoles: analysis, **topoisomerase** I inhibitor, enzyme inhibitor; **rebeccamycin** derivatives: analysis, pharmaceutical, antitumor antibiotic, cross-resistance; DNA-**topoisomerase** I covalent complex: analysis, structural elements; F361S: analysis, camptothecin-resistant **topoisomerase** I mutant; R-3: analysis, **topoisomerase** I inhibitor, **rebeccamycin** analogue, pharmaceutical, enzyme inhibitor

RN 7689-03-4 (CAMPTOTHECIN)
80449-01-0 (**TOPOISOMERASE**)
93908-02-2D (**REBECCAMYCIN**)
143180-75-0 (DNA-**TOPOISOMERASE** I)

L3 ANSWER 10 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:334340 BIOSIS
DN PREV199900334340
TI Calories from carbohydrates: Energetic contribution of the carbohydrate moiety of **rebeccamycin** to DNA binding and the effect of its orientation on **topoisomerase** I inhibition.
AU Bailly, Christian (1); Qu, Xiaogang; Graves, David E.; Prudhomme, Michelle; Chaires, Jonathan B.
CS (1) Centre Oscar Lambret et INSERM U-524, Lille, 59045 France
SO Chemistry & Biology (London), (**May, 1999**) Vol. 6, No. 5, pp. 277-286.
ISSN: 1074-5521.
DT Article
LA English
SL English
TI Calories from carbohydrates: Energetic contribution of the carbohydrate moiety of **rebeccamycin** to DNA binding and the effect of its orientation on **topoisomerase** I inhibition.
SO Chemistry & Biology (London), (**May, 1999**) Vol. 6, No. 5, pp. 277-286.
ISSN: 1074-5521.
AB Background: Only a few antitumor drugs inhibit the DNA breakage-reunion reaction catalyzed by **topoisomerase**. One is the camptothecin derivative topotecan that has recently been used clinically. Others are the glycosylated antibiotic **rebeccamycin** and its synthetic analog NB-506, which is presently in phase I of clinical trials. Unlike the camptothecins, **rebeccamycin**-type compounds bind to DNA. We set out to elucidate the molecular basis of their interaction with duplex DNA, with particular emphasis on the role of the carbohydrate residue. Results: We compared the DNA-binding and **topoisomerase** -I-inhibition activities of two isomers of **rebeccamycin** that contain a galactose residue attached to the indolocarbazole chromophore via an alpha (axial) or a beta (equatorial) glycosidic linkage. The modification of the stereochemistry of the chromophore-sugar linkage results in a marked change of the DNA-binding and **topoisomerase** I poisoning activities. The inverted configuration at the C-1' of the carbohydrate residue abolishes intercalative binding of the drug to DNA thereby drastically reducing the binding affinity. Consequently, the alpha isomer has lost the capacity to induce **topoisomerase**-I-mediated cleavage of DNA. Comparison with the aglycone allowed us to determine the energetic contribution of the sugar residue. Conclusions: The optimal interaction of **rebeccamycin** analogs with DNA is controlled to a large extent by the stereochemistry of the sugar residue. The results clarify the role of carbohydrates in stereospecific drug-DNA interactions and provide valuable information for the rational design of new **rebeccamycin**-type antitumor agents.
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques; Pharmacology
IT Chemicals & Biochemicals

carbohydrate; **rebeccamycin**: DNA-binding, antibiotic, **topoisomerase** I inhibitor; **topoisomerase** I: inhibition

RN 93908-02-2 (**REBECCAMYCIN**)
80449-01-0 (**TOPOISOMERASE**)

L3 ANSWER 11 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:184537 BIOSIS
DN PREV199900184537
TI Molecular basis for the stabilization of **topoisomerase** I-DNA covalent complexes by antitumor **rebeccamycin** analogs.
AU Carrasco, C. (1); Rubin, E.; Prudhomme, M.; Hamy, F.; Bailly, C.
CS (1) INSERM U-124, Lille France
SO Proceedings of the American Association for Cancer Research Annual Meeting, (**March, 1999**) Vol. 40, pp. 113.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research
. ISSN: 0197-016X.
DT Conference
LA English
TI Molecular basis for the stabilization of **topoisomerase** I-DNA covalent complexes by antitumor **rebeccamycin** analogs.
SO Proceedings of the American Association for Cancer Research Annual Meeting, (**March, 1999**) Vol. 40, pp. 113.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA. . .
IT Major Concepts
Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
camptothecin: antineoplastic - drug; **rebeccamycin**: antineoplastic - drug; sodium chloride; **topoisomerase** I
RN 80449-01-0 (**TOPOISOMERASE**)
93908-02-2 (**REBECCAMYCIN**)
7647-14-5 (SODIUM CHLORIDE)
7689-03-4 (CAMPTOTHECIN)

L3 ANSWER 12 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:150408 BIOSIS
DN PREV199900150408
TI Syntheses and biological activities of rebeccamycin analogues. Introduction of a halogenoacetyl substituent.
AU Moreau, Pascale; Anizon, Fabrice; Sancelme, Martine; Prudhomme, Michelle (1); Bailly, Christian; Severe, Daniele; Riou, Jean-Francois; Fabbro, Doriano; Meyer, Thomas; Aubertin, Anne-Marie
CS (1) Univ. Blaise Pascal, Synthese Electrosynthese Etude Syst. Interet Biol., UMR 6504 du CNRS, 63177 Aubiere France
SO Journal of Medicinal Chemistry, (**Feb. 25, 1999**) Vol. 42, No. 4, pp. 584-592.
ISSN: 0022-2623.
DT Article
LA English
SO Journal of Medicinal Chemistry, (**Feb. 25, 1999**) Vol. 42, No. 4, pp. 584-592.
ISSN: 0022-2623.
AB In the course of structure-activity relationships on **rebeccamycin** analogues, a series of compounds bearing a halogenoacetyl substituent were synthesized with the expectation of increasing the interaction with DNA, possibly via covalent reaction with the double helix. Two **rebeccamycin** analogues bearing an acetyl instead of a bromoacetyl substituent were prepared to gain an insight into the role of the. . . little effect on protein kinase C and no covalent reaction with DNA was detected. However, the drugs behave as typical **topoisomerase** I poisons, and they are significantly more toxic toward P388 leukemia cells

than to P388/CPT5 cells resistant to camptothecin. The introduction of a bromo- or chloro-acetyl substituent does not affect the capacity of the drug to interfere with **topoisomerase** I either in vitro or in cells. One of the bromoacetyl derivatives, compound 8, is the most cytotoxic **rebeccamycin** derivative among the hundred of derivatives we have synthesized to date. In addition, we determined the antimicrobial activities against two. . .

L3 ANSWER 13 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:150254 BIOSIS
DN PREV199900150254
TI Enhanced binding to DNA and **topoisomerase** I inhibition by an analog of the antitumor antibiotic **rebeccamycin** containing an amino sugar residue.
AU Bailly, Christian (1); Qu, Xiaogang; Anizon, Fabrice; Prudhomme, Michelle; Riou, Jean-Francois; Chaires, Jonathan B.
CS (1) IRCL, U-124 Inst. National Sante Recherche Med., Place de Verdun, 59045 Lille France
SO Molecular Pharmacology, (**Feb., 1999**) Vol. 55, No. 2, pp. 377-385.
ISSN: 0026-895X.
DT Article
LA English
TI Enhanced binding to DNA and **topoisomerase** I inhibition by an analog of the antitumor antibiotic **rebeccamycin** containing an amino sugar residue.
SO Molecular Pharmacology, (**Feb., 1999**) Vol. 55, No. 2, pp. 377-385.
ISSN: 0026-895X.
AB. . . to a DNA-intercalating chromophore. This is the case with anthracyclines such as daunomycin and also with indolocarbazoles including the antibiotic **rebeccamycin** and its tumor active analog, NB506. In each case, the glycoside residue plays a significant role in the interaction of. . . drug with the DNA double helix. In this study we show that the DNA-binding affinity and sequence selectivity of a **rebeccamycin** derivative can be enhanced by replacing the glucose residue with a 2'-aminoglucose moiety. The drug-DNA interactions were studied by thermal. . . but does not appear to participate in any specific molecular contacts. The energetic contribution of the amino group of the **rebeccamycin** analog was found to be weaker than that of the sugar amino group of daunomycin, possibly because the indolocarbazole derivative is only partially charged at neutral pH. **Topoisomerase** I-mediated DNA cleavage studies reveal that the OHfwdarwNH2 substitution does not affect the capacity of the drug to stabilize enzyme-DNA covalent complexes. Cytotoxicity studies with P388 leukemia cells sensitive or resistant to camptothecin suggest that **topoisomerase** I represents a privileged intracellular target for the studied compounds. The role of the sugar amino group is discussed. The. . .
IT Major Concepts
Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
amino sugar residue; daunomycin: antineoplastic - drug; **rebeccamycin**: antineoplastic - drug, derivative; **topoisomerase** I: inhibition; DNA
RN 80449-01-0 (**TOPOISOMERASE**)
93908-02-2 (**REBECCAMYCIN**)
20830-81-3 (DAUNOMYCIN)

L3 ANSWER 14 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:275975 BIOSIS
DN PREV199800275975
TI Syntheses and biological evaluation of indolocarbazoles, analogues of rebeccamycin, modified at the imide heterocycle.
AU Moreau, Pascale; Anizon, Fabrice; Sancelme, Martine; Prudhomme, Michelle

(1); Bailly, Christian; Carrasco, Carolina; Ollier, Monique; Severe, Daniele; Riou, Jean-Francois; Fabbro, Doriano; Meyer, Thomas; Aubertin, Anne-Marie

CS (1) Synthese Etude Syst. Interet Biol., Univ. Blaise Pascal, UMR 6504 du CNRS, 63177 Aubiere France

SO Journal of Medicinal Chemistry, (**May 7, 1998**) Vol. 41, No. 10, pp. 1631-1640.
ISSN: 0022-2623.

DT Article

LA English

SO Journal of Medicinal Chemistry, (**May 7, 1998**) Vol. 41, No. 10, pp. 1631-1640.
ISSN: 0022-2623.

AB A series of 10 indolocarbazole derivatives, analogues to the antitumor antibiotic **rebeccamycin**, bearing modifications at the imide heterocycle were synthesized. They bear an N-methyl imide, N-methyl amide, or anhydride function instead of the original imide. Their inhibitory potencies toward **topoisomerase** I were examined using a DNA relaxation assay and by analyzing the drug-induced cleavage of 32P-labeled DNA. Protein kinase C. . . as their antiviral activities toward HIV-1. The efficiency of the anhydride compounds was compared to that of the parent compound **rebeccamycin** and its dechlorinated analogue. All the compounds studied were inactive against PKC. The structural requirements for PKC and **topoisomerase** I inhibition are markedly different. In sharp contrast with the structure-PKC inhibition relationships, we found that an anhydride function does not affect **topoisomerase** I inhibition, whereas a methyl group on the indole nitrogen prevents the poisoning of **topoisomerase** I. The compounds exhibiting a marked toxicity to P388 leukemia cells had little or no effect on the growth of P388CPT5 cells which are resistant to the **topoisomerase** I inhibitor camptothecin. This study reinforces the conclusion that the DNA-**topoisomerase** I cleavable complex is the primary cellular target of the indolocarbazoles and significantly contributes to their cytotoxicity and possibly to. . .

L3 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1998:123906 BIOSIS

DN PREV199800123906

TI Recognition of specific sequences in DNA by a **topoisomerase** I inhibitor derived from the antitumor drug **rebeccamycin**.

AU Bailly, Christian (1); Colson, Pierre; Houssier, Claude; Rodrigues-Pereira, Elisabete; Prudhomme, Michelle; Waring, Michael J.

CS (1) IRCL-INSERM U124, Place de Verdun, 59045 Lille cedex France

SO Molecular Pharmacology, (**Jan., 1998**) Vol. 53, No. 1, pp. 77-87.
ISSN: 0026-895X.

DT Article

LA English

TI Recognition of specific sequences in DNA by a **topoisomerase** I inhibitor derived from the antitumor drug **rebeccamycin**.

SO Molecular Pharmacology, (**Jan., 1998**) Vol. 53, No. 1, pp. 77-87.
ISSN: 0026-895X.

AB We investigated the interaction with DNA of two synthetic derivatives of the antitumor antibiotic **rebeccamycin**: R-3, which is a potent **topoisomerase** I inhibitor and contains a methoxyglucose moiety appended to the indolocarbazole chromophore, and its aglycone, R-4. Spectroscopic measurements indicate that. . . a methyl group to pyrimidine residues suffices to create new drug binding sites. Therefore, unlike most DNA-binding small molecules, the **rebeccamycin** analogue seems to be highly sensitive to any modification of the exocyclic substituents on the bases in both the major. . . recognize their preferred GpT and TpG sites via intercalation from the major groove. The unique DNA binding characteristics of the **rebeccamycin** analogue correlate well with its inhibitory effects on **topoisomerase** I.

IT Major Concepts

Pharmacology
IT Chemicals & Biochemicals
rebeccamycin: DNA sequence recognition, antineoplastic - drug, enzyme inhibitor - drug, pharmacodynamics; **topoisomerase** [I]; DNA
RN 93908-02-2 (**REBECCAMYCIN**)
80449-01-0 (**TOPOISOMERASE**)

L3 ANSWER 16 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:505742 BIOSIS
DN PREV199799804945
TI Syntheses and biological activities (**topoisomerase** inhibition and antitumor and antimicrobial properties) of **rebeccamycin** analogues bearing modified sugar moieties and substituted on the imide nitrogen with a methyl group.
AU Anizon, Fabrice; Belin, Laure; Moreau, Pascale; Sancelme, Martine; Voldoire, Aline; Prudhomme, Michelle (1); Ollier, Monique; Severe, Daniele; Riou, Jean-Francois; Bailly, Christian; Fabbro, Dorano; Meyer, Thomas
CS (1) Synthese Electrosynthese, Etude Syst. Interet Biol., Univ. Blaise Pascal, UMR 6504, 63177 Aubiere France
SO Journal of Medicinal Chemistry, (1997) Vol. 40, No. 21, pp. 3456-3465. ISSN: 0022-2623.
DT Article
LA English
TI Syntheses and biological activities (**topoisomerase** inhibition and antitumor and antimicrobial properties) of **rebeccamycin** analogues bearing modified sugar moieties and substituted on the imide nitrogen with a methyl group.
SO Journal of Medicinal Chemistry, (1997) Vol. 40, No. 21, pp. 3456-3465. ISSN: 0022-2623.
AB As a part of studies on structure-activity relationships, several potential **topoisomerase** I inhibitors were prepared. Different analogues of the antitumor antibiotic **rebeccamycin** substituted on the imide nitrogen with a methyl group were synthesized. These compounds bore either the sugar residue or **rebeccamycin**, with or without the chlorine atoms on the indole moieties, or modified sugar residues (galactopyranosyl, glucopyranosyl, or fucopyranosyl) linked to the aglycone via a beta- or alpha-N-glycosidic bond. Their inhibitory properties toward protein kinase C, **topoisomerase** I, and **topoisomerase** II were examined, and their DNA-binding properties were investigated. Their in vitro antitumor activities against murine B16 melanoma and P388. . . Gram-positive bacteria Bacillus cereus and Streptomyces chartreusis, Gram-negative bacterium Escherichia coli, and yeast Candida albicans. These compounds are inactive toward **topoisomerase** II but inhibit **topoisomerase** I. A substitution with a methyl group on the imide nitrogen led to a loss of protein kinase C inhibition in the maleimide indolocarbazole series but did not prevent **topoisomerase** I inhibition. Compounds possessing a beta-N-glycosidic bond, which fully intercalated into DNA, were more efficient at inhibiting **topoisomerase** I than their analogues with an alpha-N-glycosidic bond; however, both were equally toxic toward P388 leukemia cells. Dechlorinated **rebeccamycin** possessing a methyl group on the imide nitrogen was about 10 times more efficient in terms of cytotoxicity and inhibition of **topoisomerase** I than the natural metabolite.
IT . . .
Biology; Enzymology (Biochemistry and Molecular Biophysics); Infection; Integumentary System (Chemical Coordination and Homeostasis); Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
TOPOISOMERASE; REBECCAMYCIN; TOPOISOMERASE II; PROTEIN KINASE C
IT Miscellaneous Descriptors

ANTIBACTERIAL-DRUG; ANTIFUNGAL-DRUG; ANTINEOPLASTIC-DRUG; BIOBUSINESS; DNA; ENZYME INHIBITOR-DRUG; INFECTION; MURINE LEUKEMIA; MURINE MELANOMA; PHARMACEUTICALS; PHARMACOLOGY; PROTEIN KINASE C; **REBECCAMYCIN**; **TOPOISOMERASE** I; **TOPOISOMERASE** II; TUMOR BIOLOGY

RN 80449-01-0 (**TOPOISOMERASE**)
93908-02-2 (**REBECCAMYCIN**)
142805-56-9 (**TOPOISOMERASE** II)
141436-78-4 (PROTEIN KINASE C)

L3 ANSWER 17 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:216118 BIOSIS
DN PREV199799522622
TI DNA cleavage by **topoisomerase** I in the presence of indolocarbazole derivatives of **rebeccamycin**.
AU Bailly, Christian (1); Riou, Jean-Francois; Colson, Pierre; Houssier, Claude; Rodrigues-Pereira, Elisabete; Prudhomme, Michelle
CS (1) INSERM U124, Lab. Pharmacologie Moleculaire Antitumorale, Centre Oscar Lambret, Inst. Rech. Cancer, Place de Verdun, 59045 Lille France
SO Biochemistry, (1997) Vol. 36, No. 13, pp. 3917-3929.
ISSN: 0006-2960.
DT Article
LA English
TI DNA cleavage by **topoisomerase** I in the presence of indolocarbazole derivatives of **rebeccamycin**.
SO Biochemistry, (1997) Vol. 36, No. 13, pp. 3917-3929.
ISSN: 0006-2960.
AB DNA **topoisomerase** I has been shown to be an important therapeutic target in cancer chemotherapy for the camptothecins as well as for. . . . and its synthetic derivatives NB-506 and ED-110 (Yoshinari et al. (1993) Cancer Res. 53, 490-494). To investigate the mechanism of **topoisomerase** I inhibition by indolocarbazoles, we have studied the induction of DNA cleavage by purified mammalian **topoisomerase** I mediated by the antitumor antibiotic **rebeccamycin** and a series of 20 indolocarbazole derivatives. The compounds tested bear (i) various functional groups on the non-indolic moiety (X. . . . on the maleimido function (R-1 = H, OH, NH-2, NHCHO). Half of the ligands have the same carbohydrate moiety as **rebeccamycin** whereas the other ligands have no sugar residue. The inhibitory potency of the test compounds was assessed in vitro by. . . study shows that the sugar residue attached to the indolocarbazole chromophore is critical for the drug ability to interfere with **topoisomerase** I as well as for the formation of intercalation complexes. Structure-activity relationships indicate that the presence of chlorine atoms significantly reduces the effects on **topoisomerase** I whereas the substituents on the maleimido function and the functional group on the non-indolic moiety can be varied without reduction of activity. The results suggest that the inhibition of **topoisomerase** I by indolocarbazoles arises in part from their ability to interact with DNA. Analysis of the base preferences around **topoisomerase** I cleavage sites in various restriction fragments indicated that, in a manner similar to camptothecin, the **rebeccamycin** analogue R-3 stabilized **topoisomerase** I preferentially at sites having a T and a G on the 5' and 3' sides of the cleaved bond, respectively. By analogy with models previously proposed for camptothecin and numerous **topoisomerase** II inhibitors which intercalate into DNA, a stacking model for the interaction between DNA, **topoisomerase** I and indolocarbazoles is proposed. These findings provide guidance for the development of new **topoisomerase** I-targeted antitumor indolocarbazole derivatives.
IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
TOPOISOMERASE; **REBECCAMYCIN**; DNA

TOPOISOMERASE I; **REBECCAMYCIN**
IT Miscellaneous Descriptors
ANTINEOPLASTIC-DRUG; CLEAVAGE; DNA; DNA **TOPOISOMERASE** I; ENZYME INHIBITOR-DRUG; ENZYMOLOGY; INDOLOCARBAZOLE DERIVATIVES; PHARMACOLOGY; **REBECCAMYCIN**
RN 80449-01-0 (**TOPOISOMERASE**)
93908-02-2D (**REBECCAMYCIN**)
143180-75-0 (DNA **TOPOISOMERASE** I)
93908-02-2 (**REBECCAMYCIN**)

L3 ANSWER 18 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:541885 BIOSIS
DN PREV199699264241
TI Structure-activity relationships in a series of substituted indolocarbazoles: Topoisomerase I and protein kinase C inhibition and antitumoral and antimicrobial properties.
AU Pereira, Elisabete Rodrigues; Belin, Laure; Sancelme, Martine; Prudhomme, Michelle (1); Ollier, Monique; Rapp, Maryse; Severe, Daniele; Riou, Jean-Francois; Fabbro, Doriano; Meyer, Thomas
CS (1) Synthese Etude System Interet Biol., Univ. Blaise Pascal, URA 485 du CNRS, 63177 Aubiere France
SO Journal of Medicinal Chemistry, (1996) Vol. 39, No. 22, pp. 4471-4477. ISSN: 0022-2623.
DT Article
LA English
SO Journal of Medicinal Chemistry, (1996) Vol. 39, No. 22, pp. 4471-4477. ISSN: 0022-2623.
AB A series of compounds structurally related to staurosporine, **rebeccamycin**, and corresponding aglycones was synthesized, and their activities toward protein kinase C and topoisomerases I and II were tested together. . . . on the maleimide nitrogen and/or a sugar moiety linked to one of the indole nitrogens to obtain specific inhibitors of **topoisomerase** I with minimal activities on protein kinase C. As expected, these structures were inefficient on **topoisomerase** II, and some of them exhibited a strong activity against **topoisomerase** I. Generally, dechlorinated compounds were found to be more active than chlorinated analogues against both purified **topoisomerase** I and protein kinase C. On the other hand, opposite results were obtained in the cell antiproliferative assays. These results. . .

L3 ANSWER 19 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1988:344448 BIOSIS
DN BR35:39290
TI IDENTIFICATION AND CHARACTERIZATION OF NOVEL TOPOISOMERASE INHIBITORS.
AU LONG B H; JIMENEZ N E; MUSIAL S T; CASAZZA A M
CS CANCER RES., PHARMACEUTICAL RES. AND DEV., BRISTOL-MEYERS, WALLINGFORD, CONN. 06492.
SO 79TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW ORLEANS, LOUISIANA, USA, MAY 25-28, 1988. PROC AM ASSOC CANCER RES ANNU MEET. (1988) 29 (0), 270.
CODEN: PAMREA.
DT Conference
FS BR; OLD
LA English
SO 79TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW ORLEANS, LOUISIANA, USA, MAY 25-28, 1988. PROC AM ASSOC CANCER RES ANNU MEET. (1988) 29 (0), 270.
CODEN: PAMREA.
RN 6377-18-0 (CHARTREUSIN)
7689-03-4 (CAMPTOTHECIN)
23214-92-8 (DOXORUBICIN)
29767-20-2 (TENIPOSIDE)
77879-90-4 (GILVOCARCIN V)
80449-01-0 (**TOPOISOMERASE**)

83138-95-8 (VIRENOMYCIN V)
83138-96-9 (VIRENOMYCIN M)
93908-02-2 (**REBECCAMYCIN**)

L3 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:459763 CAPLUS
DN 133:222613
TI Recent developments in the synthesis of indolocarbazoles, topoisomerase I inhibitors
AU Prudhomme, M.; Anizon, F.; Moreau, P.
CS Laboratoire .mchlt. Synthese, Electrosynthese et Etude de Systemes a Interet Biologique .mchgt., UMR 6504, Laboratoire .mchlt. Synthese, Electrosynthese et Etude de Systemes a Interet Biologique .mchgt., UMR 6504, Universite Blaise Pascal-CNRS, Aubiere, 63177, Fr.
SO Recent Research Developments in Synthetic Organic Chemistry (**1999**), 2, 79-106
CODEN: RDSCF5
PB Transworld Research Network
DT Journal; General Review
LA English
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Recent Research Developments in Synthetic Organic Chemistry (**1999**), 2, 79-106
CODEN: RDSCF5
IT 93908-02-2P, **Rebeccamycin**
RL: SPN (Synthetic preparation); PREP (Preparation)
(related compds.; recent developments in synthesis of indolocarbazole **topoisomerase** I inhibitors)

L3 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:220889 CAPLUS
DN 133:114678
TI Recognition and cleavage of DNA by rebeccamycin- or benzopyridoquinoxaline conjugated of triple helix-forming oligonucleotides
AU Arimondo, P. B.; Moreau, P.; Boutorine, A.; Bailly, C.; Prudhomme, M.; Sun, J.-S.; Garestier, T.; Hélène, C.
CS INSERM U201, UMR 8646 CNRS-Museum National d'Histoire Naturelle, Laboratoire de Biophysique, Paris, 75231, Fr.
SO Bioorganic & Medicinal Chemistry (**2000**), 8(4), 777-784
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Bioorganic & Medicinal Chemistry (**2000**), 8(4), 777-784
CODEN: BMECEP; ISSN: 0968-0896
ST **rebeccamycin** oligonucleotide conjugate DNA cleavage **topoisomerase**; benzopyridoquinoxaline oligonucleotide conjugate DNA cleavage **topoisomerase**

L3 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:585185 CAPLUS
DN 127:271977
TI Indolocarbazoles as anti-cancer agents
AU Prudhomme, Michelle
CS Synthese, Electrosynthese et Etudes de Systemes a Interet Biologique, Univ. Blaise Pascal, Aubiere, 63177, Fr.
SO Current Pharmaceutical Design (**1997**), 3(3), 265-290
CODEN: CPDEFP; ISSN: 1381-6128
PB Bentham Science Publishers
DT Journal; General Review
LA English

SO Current Pharmaceutical Design (**1997**), 3(3), 265-290
CODEN: CPDEFP; ISSN: 1381-6128

AB A review with 142 refs. Protein kinase C (PKC) is a family of phospholipid-dependent serine/threonine protein kinases that plays a key role in signal transduction. Consequently, PKC controls a large variety of cellular processes such as proliferation and differentiation as well as smooth muscle contraction and secretions. The disruption of these processes would have severe implications for many physiol. functions. The twelve known PKC isoenzymes show great variations in their substrate specificity and their distribution among different tissues, indicating their specialized role in certain tissue functions. Altered expression of PKC isoenzymes has been reported in a wide range of diseases. DNA **topoisomerase** I is a nuclear enzyme, involved in replication, transcription and recombination, that modifies and regulates the topol. state of DNA. Many microbial metabolites and synthetic compds. possessing an indolocarbazole unit are biol. active products with antitumor properties. Antibiotic indolocarbazoles staurosporine, K-252a, UCN-01 and 02 are known protein kinase C inhibitors while structurally related **rebeccamycin** and ED-110 are **topoisomerase** I inhibitors without inhibitory effect against PKC. This review will update efforts made toward the discovery of antitumor indolocarbazoles and their possible mode of action via either PKC or **topoisomerase** I inhibition. Structure-activity relation studies in a series of maleamide and maleimide indolocarbazoles bearing or not a sugar moiety linked either to both indole nitrogens such as staurosporine, or to one indole nitrogen such as **rebeccamycin**, will be reported.

L3 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:32620 CAPLUS
DN 118:32620
TI Induction of mammalian DNA topoisomerase I mediated DNA cleavage by antitumor indolocarbazole derivatives
AU Yamashita, Yoshinori; Fujii, Noboru; Murakata, Chikara; Ashizawa, Tadashi; Okabe, Masami; Nakano, Hirofumi
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Machida, 194, Japan
SO Biochemistry (**1992**), 31(48), 12069-75
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
SO Biochemistry (**1992**), 31(48), 12069-75
CODEN: BICHAW; ISSN: 0006-2960
IT 7689-03-4, Camptothecin 93908-02-2, **Rebeccamycin** 99533-80-9, K252a 112953-11-4, UCN-01 145253-49-2, KT 6661
RL: BIOL (Biological study)
(DNA **topoisomerase** I-mediated DNA cleavage response to, neoplasm inhibition in relation to)

L3 ANSWER 24 OF 29 DRUGNL COPYRIGHT 2003 IMSWORLD on STN

AN 1999:1558 DRUGNL
TI IXL 119 National Cancer Institute clinical data
SO R&D Focus Drug News (**7 Jun 1999**).
WC 238
SO R&D Focus Drug News (**7 Jun 1999**).
TX Data on NSC 655649 (BMY 27557), a water soluble **rebeccamycin** analogue in development with the US National Cancer Institute (NCI), were presented at the 35th Annual Meeting of the American Society of Clinical Oncology, 15-18 May 1999, Atlanta, USA. The agent, a **topoisomerase** II inhibitor and DNA intercalator, was assessed in 18 patients with advanced gallbladder and other cancers at the University Hospitals. . .

L3 ANSWER 25 OF 29 COPYRIGHT 2003 Gale Group on STN

AN 97:1234 NLDB
TI Drug Development "Structure-Activity Relationships in a Series of Substituted Indolocarbazoles: Topoisomerase I and Protein Kinase C Inhibition and Antitumoral and Antimicrobial Properties."
SO Cancer Weekly Plus, (**6 Jan 1997**) .
PB Charles W Henderson
DT Newsletter
LA English
WC 274
SO Cancer Weekly Plus, (**6 Jan 1997**) .
TX According . . . the authors' abstract of an article published in Journal of Medicinal Chemistry, "A series of compounds structurally related to staurosporine, **rebeccamycin**, and corresponding aglycones was synthesized, and their activities toward protein kinase C and topoisomerases I and II were tested together. . . on the maleimide nitrogen and/or a sugar moiety linked to one of the indole nitrogens to obtain specific inhibitors of **topoisomerase** I with minimal activities on protein kinase C. As expected, these structures were inefficient on **topoisomerase** II, and some of them exhibited a strong activity against **topoisomerase** I. Generally, dechlorinated compounds were found to be more active than chlorinated analogues against both purified **topoisomerase** I and protein kinase C. On the other hand, opposite results were obtained in the cell antiproliferative assays. These results. . .

L3 ANSWER 26 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 1999:872581 SCISEARCH
GA The Genuine Article (R) Number: 253PJ
TI The first synthesis of the bis(indole) marine alkaloid caulersin
AU Fresneda P M (Reprint); Molina P; Saez M A
CS UNIV MURCIA, FAC QUIM, DEPT QUIM ORGAN, CAMPUS ESPINARDO, E-30071 MURCIA, SPAIN (Reprint)
CYA SPAIN
SO SYNLETT, (**OCT 1999**) No. 10, pp. 1651-1653.
Publisher: GEORG THIEME VERLAG, P O BOX 30 11 20, D-70451 STUTTGART, GERMANY.
ISSN: 0936-5214.
DT Article; Journal
FS PHYS
LA English
REC Reference Count: 23
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
SO SYNLETT, (**OCT 1999**) No. 10, pp. 1651-1653.
Publisher: GEORG THIEME VERLAG, P O BOX 30 11 20, D-70451 STUTTGART, GERMANY.
ISSN: 0936-5214.
STP KeyWords Plus (R): PROTEIN KINASE-C; DNA **TOPOISOMERASE**-I; PIGMENT CAULERPIN; **REBECCAMYCIN**; TRANSCRIPTION; DERIVATIVES

L3 ANSWER 27 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 1999:363298 SCISEARCH
GA The Genuine Article (R) Number: 188TJ
TI NB 506
AU Lansiaux A (Reprint); Bailly C
CS CTR OSCAR LAMBRET, LAB PHARMACOL ANTITUMORALE, PL VERDUN, F-59045 LILLE, FRANCE (Reprint); INSERM U524, F-59045 LILLE, FRANCE
CYA FRANCE
SO BULLETIN DU CANCER, (**MAR 1999**) Vol. 86, No. 3, pp. 255-258.
Publisher: JOHN LIBBEY EUROTEXT LTD, 127 AVE DE LA REPUBLIQUE, 92120 MONTROUGE, FRANCE.
ISSN: 0007-4551.
DT Article; Journal
FS LIFE; CLIN
LA French

REC Reference Count: 17
SO BULLETIN DU CANCER, (**MAR 1999**) Vol. 86, No. 3, pp. 255-258.
Publisher: JOHN LIBBEY EUROTEXT LTD, 127 AVE DE LA REPUBLIQUE, 92120 MONTROUGE, FRANCE.. . .
STP KeyWords Plus (R): COMPOUND 6-N-FORMYLAMINO-12,13-DIHYDRO-1,11-DIHYDROXY-13-(BETA-D-GLUCOPYRANOSYL); **TOPOISOMERASE**-I INHIBITORS; MEDIATED DNA CLEAVAGE; INDOLOCARBAZOLE DERIVATIVES; ANTITUMOR ACTIVITIES; BIOLOGICAL-ACTIVITY; TUMOR-CELLS; **REBECCAMYCIN**; SUBSTANCE; INDUCTION

L3 ANSWER 28 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 1998:1362 SCISEARCH
GA The Genuine Article (R) Number: YK872
TI A new entry to indolo[2,3-a]carbazoles
AU Beccalli E M (Reprint); Marchesini A
CS FAC FARM, IST CHIM ORGAN, VIA VENEZIAN 21, I-20133 MILAN, ITALY (Reprint)
CYA ITALY
SO SYNTHETIC COMMUNICATIONS, (**NOV 1997**) Vol. 27, No. 24, pp. 4215-4221.
Publisher: MARCEL DEKKER INC, 270 MADISON AVE, NEW YORK, NY 10016.
ISSN: 0039-7911.
DT Article; Journal
FS PHYS
LA English
REC Reference Count: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
SO SYNTHETIC COMMUNICATIONS, (**NOV 1997**) Vol. 27, No. 24, pp. 4215-4221.
Publisher: MARCEL DEKKER INC, 270 MADISON AVE, NEW YORK, NY 10016.
ISSN: 0039-7911.
STP KeyWords Plus (R): PROTEIN-KINASE-C; DNA **TOPOISOMERASE**-I; **REBECCAMYCIN**; TRANSCRIPTION

L3 ANSWER 29 OF 29 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 93:344114 SCISEARCH
GA The Genuine Article (R) Number: LD566
TI ED-110, A NOVEL INDOLOCARBAZOLE, PREVENTS THE GROWTH OF EXPERIMENTAL-TUMORS IN MICE
AU ARAKAWA H; IGUCHI T; YOSHINARI T; KOJIRI K; SUDA H; OKURA A (Reprint)
CS MERCK RES LABS, BANYU TSUKUBA RES INST, OKUBO 3, TSUKUBA 30033, JAPAN
CYA JAPAN
SO JAPANESE JOURNAL OF CANCER RESEARCH, (**MAY 1993**) Vol. 84, No. 5, pp. 574-581.
ISSN: 0910-5050.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 31
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
SO JAPANESE JOURNAL OF CANCER RESEARCH, (**MAY 1993**) Vol. 84, No. 5, pp. 574-581.
ISSN: 0910-5050.
STP KeyWords Plus (R): DNA **TOPOISOMERASE**-II; RAT-KIDNEY CELLS; BIOLOGICAL-ACTIVITY; ANTITUMOR-ACTIVITY; POTENT INHIBITOR; PROTEIN-KINASE; PROLIFERATION; CAMPTOTHECIN; **REBECCAMYCIN**; REPLICATION

L3 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
AN 2003:245064 CAPLUS
TI A Phase II Study of Rebeccamycin Analog NSC 655649 in Patients with Metastatic Colorectal Cancer
AU Goel, Sanjay; Wadler, Scott; Hoffman, Anthony; Volterra, Fabio; Baker, Cheryl; Nazario, Elliot; Ivy, Percy; Silverman, Alyson; Mani, Sridhar
CS Department of Oncology, Montefiore Medical Center, Bronx, NY, 10461, USA
SO Investigational New Drugs (2003), 21(1), 103-107
CODEN: INNDDK; ISSN: 0167-6997
PB Kluwer Academic Publishers
DT Journal
LA English
AB The analog, **rebeccamycin** tartrate salt (NSC 655649, Cancer Therapy Evaluation Program, National Cancer Institute) has broad preclin. anti-**neoplastic** activity. Preliminary data from phase I study demonstrated anti-tumor activity in colorectal carcinoma. This phase II trial evaluates its efficacy in patients with minimally treated metastatic colorectal cancer. Eligibility included Karnofsky performance status .gtoreq.70%, age .gtoreq.18 yr and bidimensionally measurable disease. Thirteen patients were treated with NSC 655649 at 500 mg/m2 by central venous catheter once every 3 wk by bolus injection. Thirty-four cycles (median [range] 2 [1-6]) of therapy were administered. Twelve patients are eligible for response assessment. No major objective responses were seen using the RECIST criteria; however stable disease was obsd. in three patients with mean duration of 15 wk. The median time to progression was 8 wk. There was no toxic death. Four patients received only one cycle of treatment, and three had disease progression. Toxicities were tolerable and hematol. toxicity was the most common. The median (range) granulocyte and platelet nadir counts were 2043/.mu.l (116-16,374/.mu.l) and 276.times.103/.mu.l (5-769), resp. Non-hematol. toxicities were moderate, including generalized weakness/fatigue, nausea/vomiting, diarrhea and anorexia. One patient required dose redn.; three patients required dose delays. NSC 655649 at this dose and schedule is inactive against advanced previously minimally treated metastatic colorectal cancer and further study of this drug as a single agent in this disease using an every three-week schedule is not warranted.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 7 CANCERLIT on STN DUPLICATE 2
AN 2002056539 CANCERLIT
DN 21281045 PubMed ID: 11387367
TI Phase I and pharmacokinetic study of NSC 655649, a rebeccamycin analog with topoisomerase inhibitory properties.
AU Tolcher A W; Eckhardt S G; Kuhn J; Hammond L; Weiss G; Rizzo J; Aylesworth C; Hidalgo M; Patnaik A; Schwartz G; Felton S; Campbell E; Rowinsky E K
CS Institute for Drug Development, Cancer Therapy and Research Center, San Antonio, Texas 78229, USA.. atolcher@saci.org
NC 5P30 CA54174 (NCI)
MO1 RR01346-19 (NCRR)
U01 CA69853 (NCI)
SO JOURNAL OF CLINICAL ONCOLOGY, (2001 Jun 1) 19 (11) 2937-47.
Journal code: 8309333. ISSN: 0732-183X.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2001314208
EM 200107
ED Entered STN: 20020726
Last Updated on STN: 20020726

AB PURPOSE: To assess the feasibility of administering NSC 655649, a water-soluble, **rebeccamycin** analog with topoisomerase inhibitory properties, as a brief intravenous (IV) infusion once every 3 weeks and to determine the maximum-tolerated dose (MTD) of NSC 655649, characterize its pharmacokinetic behavior, and seek preliminary evidence of antitumor activity. PATIENTS AND METHODS: Patients with advanced solid malignancies were treated with escalating doses of NSC 655649 administered over 30 to 60 minutes IV once every 3 weeks. An accelerated dose-escalation method was used to guide dose escalation. After three patients were treated at the first dose level, doses were escalated in increments that ranged up to 150% using single patient cohorts until moderate toxicity was observed, when a more conservative dose-escalation scheme was invoked. MTD was defined as the highest dose level at which the incidence of dose-limiting toxicity did not exceed 20%. MTD was determined for both minimally pretreated (MP) and heavily pretreated (HP) patients. Plasma and urine were sampled to characterize the pharmacokinetic and excretory behavior of NSC 655649. RESULTS: Forty-five patients were treated with 130 courses of NSC 655649 at doses ranging from 20 mg/m(2) to 744 mg/m(2). Myelosuppression was the principal toxicity. Severe neutropenia, which was often associated with thrombocytopenia, was unacceptably high in HP and MP patients treated at 572 mg/m(2) and 744 mg/m(2), respectively. Nausea, vomiting, and diarrhea were common but rarely severe. The pharmacokinetics of NSC 655649 were dose dependent and fit a three-compartment model. The clearance and terminal elimination half-lives for NSC 655649 averaged 7.57 (SD = 4.2) L/h/m(2) and 48.85 (SD = 23.65) hours, respectively. Despite a heterogeneous population of MP and HP patients, the magnitude of drug exposure correlated well with the severity of myelosuppression. Antitumor activity was observed in two HP ovarian cancer patients and one patient with a soft tissue sarcoma refractory to etoposide and doxorubicin. CONCLUSION: Recommended phase II doses are 500 mg/m(2) and 572 mg/m(2) IV once every 3 weeks for HP and MP patients, respectively. The absence of severe nonhematologic toxicities, the encouraging antitumor activity in HP patients, and the unique mechanism of **antineoplastic** activity of NSC 655649 warrant further clinical development.

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
AN 2001:829938 CAPLUS
DN 136:112106
TI Design of new anti-cancer agents based on topoisomerase poisons targeted to specific DNA sequences
AU Arimondo, P. B.; Helene, C.
CS Laboratoire de Biophysique, Museum National d'Histoire Naturelle, UMR8646 CNRS, INSERM U201, Paris, 75005, Fr.
SO Current Medicinal Chemistry: Anti-Cancer Agents (2001), 1(3), 219-235 CODEN: CMCACI; ISSN: 1568-0118
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
AB A review. There is considerable interest in the development of sequence-selective DNA drugs. Chem. agents able to interfere with DNA topoisomerases - essential nuclear enzymes- are widespread in nature, and some of them have outstanding therapeutic efficacy in human cancer and infectious diseases. Several classes of **antineoplastic** drugs, such as amsacrine, daunorubicin, etoposide (acting on type II topoisomerases), camptothecin and indolocarbazole derivs. of the antibiotic **rebeccamycin** (acting on type IB topoisomerases), have been shown to stimulate DNA cleavage by topoisomerases leading to cell death. However, these mols. exhibit little sequence preference. A convenient strategy to confer sequence specificity consists in the attachment of these topoisomerase poisons to sequence-specific DNA binding elements. Among sequence-specific DNA ligands, oligonucleotides can bind with high specificity of recognition to the major groove of double-helical DNA, resulting in triple helix formation. In this context, derivs. of camptothecin, indolocarbazole, anthracycline and acridine poisons have

been covalently tethered to triple helix-forming oligonucleotides. The use of triple-helical DNA structures offers an efficient system to target topoisomerase I and II-mediated DNA cleavage to specific sequences and to increase the drug efficacy at these sites. Chem. optimization of the conjugates is essential to the efficacy of drug targeting. Consequently, the rational design of this new class of anticancer agents, conceived from topoisomerase poisons and triplex-forming oligonucleotides, may be exploited to improve the efficacy and selectivity of the DNA damage induced by topoisomerases.

RE.CNT 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 7 USPATFULL on STN
AN 92:89049 USPATFULL
TI Rebeccamycin
IN Lam, Kin S., Cheshire, CT, United States
Schroeder, Daniel R., Higganum, CT, United States
Mattei, Jacqueline, Branford, CT, United States
Matson, James A., Chesire, CT, United States
Forenza, Salvatore, Chesire, CT, United States
PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)
PI US 5158938 19921027
AI US 1991-764116 19910923 (7)
RLI Continuation of Ser. No. US 1990-488915, filed on 6 Mar 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: Wilson, J. Oliver
LREP Cepeda-Kaye, Michelle A.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 392
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Addition of bromine to the culture medium during fermentation of a **rebeccamycin**-producing strain of Saccharothrix aerocolonigenes results in production of a new **rebeccamycin** derivative having advantageous **antineoplastic** properties.

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
AN 1992:82213 CAPLUS
DN 116:82213
TI Bromo-analogs of rebeccamycin from fermentation of Saccharothrix
IN Lam, Kin Sing; Schroeder, Daniel R.; Mattei, Jaqueline Marie; Matson, James Andrew; Forenza, Salvatore
PA Bristol-Myers Squibb Co., USA
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 445736	A1	19910911	EP 1991-103317	19910305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2037596	AA	19910907	CA 1991-2037596	19910305
CA 2037596	C	19950718		
JP 06128282	A2	19940510	JP 1991-38282	19910305
JP 07025787	B4	19950322		
US 5158938	A	19921027	US 1991-764116	19910923
PRAI US 1990-488915		19900306		

AB A bromo-analog of **rebeccamycin** (I) is manufd. by cultures of

Saccharothrix aerocolonigenes in a medium supplemented with bromide. I is useful as a **neoplasm** inhibitor. In a 10 L fermn. in a defined medium contg. KBr 0.5 g/L yields of I reached 5.9-7.1 .mu.g/mL after 507 days fermn. at 28.degree..

L3 ANSWER 6 OF 7 USPATFULL on STN
AN 89:15075 USPATFULL
TI Rebeccamycin derivative containing pharmaceutical composition
IN Kaneko, Takushi, Guilford, CT, United States
Wong, Henry S., Durham, CT, United States
Utzig, Jacob J., Buffalo, NY, United States
PA Bristol-Myers Company, New York, NY, United States (U.S. corporation)
PI US 4808613 19890228
AI US 1988-169785 19880318 (7)
RLI Continuation of Ser. No. US 1986-933428, filed on 21 Nov 1986, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Griffin, Ronald W.; Assistant Examiner: Crane, L. Eric
LREP Morse, David M.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 490
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There are disclosed analogs of the antitumor agent, rebaccamycin, which possess **antineoplastic** properties against mammalian, particularly experimental animal, tumor systems. The compounds of the invention are aminoalkylated derivatives of **rebeccamycin** produced by first reacting **rebeccamycin** with a strong base to obtain a reactive intermediate and then reacting the reactive intermediate with an aminoalkyl compound.

L3 ANSWER 7 OF 7 USPATFULL on STN
AN 88:74145 USPATFULL
TI Rebeccamycin analogs
IN Kaneko, Takushi, Guilford, CT, United States
Wong, Henry S., Durham, CT, United States
Utzig, Jacob J., Buffalo, NY, United States
PA Bristol-Myers Company, New York, NY, United States (U.S. corporation)
PI US 4785085 19881115
AI US 1986-933428 19861121 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Griffin, Ronald W.; Assistant Examiner: Crane, L. Eric
LREP Morse, David M.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 562
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There are disclosed analogs of the antitumor agent, **rebeccamycin**, which possess **antineoplastic** properties against mammalian, particularly experimental animal, tumor systems. The compounds of the invention are aminoalkylated derivatives of **rebeccamycin** produced by first reacting **rebeccamycin** with a strong base to obtain a reactive intermediate and then reacting the reactive intermediate with an aminoalkyl compound.

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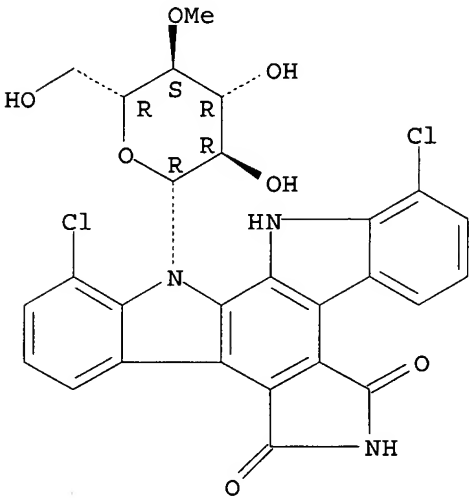
L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 93908-02-2 REGISTRY
CN 5H-Indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione,
1,11-dichloro-12,13-dihydro-12-(4-O-methyl-.beta.-D-glucopyranosyl)- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN NSC 359079
CN **Rebeccamycin**
FS STEREOSEARCH
MF C27 H21 Cl2 N3 O7
LC STN Files: ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU,
EMBASE, IPA, MEDLINE, NAPRALERT, PROMT, RTECS*, TOXCENTER, USPAT2,
USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



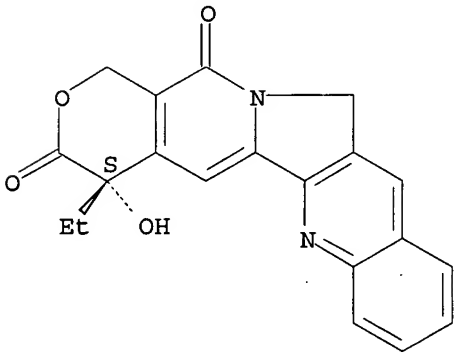
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

65 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
65 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 7689-03-4 REGISTRY
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione,
    4-ethyl-4-hydroxy-, (4S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione,
    4-ethyl-4-hydroxy-, (S)-
CN Camptothecine (7CI)
OTHER NAMES:
CN (+)-Camptothecin
CN (+)-Camptothecine
CN (S)-Camptothecin
CN 20(S)-Camptothecin
CN 20(S)-Camptothecine
CN **Camptothecin**
CN d-Camptothecin
CN NSC 94600
FS STEREOSEARCH
DR 30628-51-4, 157405-40-8
MF C20 H16 N2 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
    BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
    CHEMINFORMRX, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB,
    IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PROMT, RTECS*, SPECINFO,
    SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
      (*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2138 REFERENCES IN FILE CA (1907 TO DATE)
 281 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2152 REFERENCES IN FILE CAPLUS (1907 TO DATE)
   1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L6 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:571012 CAPLUS
DN 139:127982
TI Peptides and peptidomimetics having anti-proliferative activity and/or that augment nucleic acid damaging agents or treatments
IN Kawabe, Takumi; Kobayashi, Hidetaka
PA Canbas Research Laboratories, Ltd., Japan
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059942	A2	20030724	WO 2003-IB425	20030117

PI WO 2003059942 A2 20030724 WO 2003-IB425 20030117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-350208P P 20020117
IT Antitumor agents
Apoptosis
Bladder, neoplasm
Bone, neoplasm
Brain, neoplasm
Carcinoma
Digestive tract, neoplasm
Drug delivery systems
Gamma ray
Head, neoplasm
Hyperthermia (therapeutic)
IR **radiation**
Kidney, neoplasm
Leukemia
Liver, neoplasm
Lung, neoplasm
Lymphatic system, neoplasm
Lymphoma
Mammary gland, neoplasm
Multiple myeloma
Pancreas, neoplasm
Peptidomimetics
Radiotherapy
Sarcoma
Skin, neoplasm
Thyroid gland, neoplasm
UV **radiation**
(peptides and peptidomimetics having antitumor activity)
IT 12587-46-1, Alpha particle
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**Radiation**; peptides and peptidomimetics having antitumor activity)
IT 12587-47-2, .beta.-Particle
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Radiation**; peptides and peptidomimetics having antitumor activity)
IT 51-21-8, 5-Fluorouracil 7689-03-4, Camptothecin 11056-06-7, Bleomycin

15663-27-1, Cisplatin 25316-40-9, Adriamycin 61825-94-3, Oxaliplatin
68247-85-8, Pepleomycin **93908-02-2**, **Rebeccamycin**
565434-67-5 565434-68-6, CBP 511 565434-69-7 565434-70-0
565434-71-1 565434-72-2, CBP 510 565434-73-3, CBP 512 565434-74-4
565434-75-5 565434-76-6, CBP 608 565434-77-7, CBP 700 565434-78-8
565434-79-9, CBP 701 565434-80-2 565434-81-3, CBP 702 565434-82-4
565434-83-5, CBP 703 565434-84-6 565434-85-7, CBP 501 565434-86-8
565434-87-9 565434-88-0 565434-89-1 565434-90-4 565434-91-5
565434-92-6 565434-93-7, CBP 0 565434-94-8, CBP 451 565434-95-9, CBP
452 565434-96-0, CBP 603 565434-97-1, CBP 607 565434-98-2, CBP 609
565434-99-3 565435-00-9 565435-01-0 565435-02-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(peptides and peptidomimetics having antitumor activity)

L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:850945 CAPLUS
DN 135:366733
TI Compositions and methods for the treatment of cancer
IN Zeldis, Jerome B.; Zeitlin, Andrew; Barer, Sol
PA Celgene Corp., USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087307	A2	20011122	WO 2001-US15327	20010510
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2001010877	A	20030311	BR 2001-10877	20010510
	EP 1307197	A2	20030507	EP 2001-935373	20010510
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2002035090	A1	20020321	US 2001-853617	20010514
PRAI	US 2000-204143P	P	20000515		
	WO 2001-US15327	W	20010510		

AB This invention relates to compns. comprising thalidomide and another anti-cancer drug which can be used in the treatment or prevention of cancer. Preferred anti-cancer drugs are topoisomerase inhibitors. A particular compn. comprises thalidomide, or a pharmaceutically acceptable salt, solvate, or clathrate thereof, and irinotecan. The invention also relates to methods of treating or preventing cancer which comprise the administration of a thalidomide and another anti-cancer drug to a patient in need of such treatment or prevention. The invention further relates to methods of reducing or avoiding adverse side effects assocd. with the administration of chemotherapy or **radiation** therapy which comprise the administration of thalidomide to a patient in need of such redn. or avoidance.

IT 4707-32-8, .beta.-Lapachone 6872-57-7, Nitidine 6872-73-7, Coralyne 6873-09-2, Epiberberine 7689-03-4, Camptothecin 23491-45-4, Hoechst 33258 23491-52-3 52259-65-1, Fagaronine 62417-80-5, Bulgarein 86639-52-3, SN-38 89458-99-1, XR-5000 91421-42-0, Rubitecan 91421-43-1, 9-Aminocamptothecin **93908-02-2**, **Rebeccamycin** 97682-44-5, Irinotecan 99009-20-8, Pyrazoloacridine 123948-87-8, Topotecan 131190-63-1, Saintopin 139112-73-5, ED-110 149882-10-0,

GG-211 150829-94-0, UCE6 151069-12-4, NB-506 154163-86-7, TAN-1518A 154163-87-8, TAN-1518B 158243-10-8, UCE1022 169869-90-3, DX-8951f
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising thalidomide and irinotecan for treatment of cancer)

L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:229018 CAPLUS
DN 134:275749
TI Peptide sequences and methods for inhibiting G2 cell cycle arrest and sensitizing cells to DNA damaging agents
IN Suganuma, Masashi; Kawabe, Takumi
PA Canbas Co., Ltd., Japan
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001021771	A2	20010329	WO 2000-IB1438	20000921
	WO 2001021771	A3	20020214		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	JP 2001086991	A2	20010403	JP 1999-269398	19990922
	JP 2001157585	A2	20010612	JP 1999-340322	19991130
	EP 1218494	A2	20020703	EP 2000-964563	20000921
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003518368	T2	20030610	JP 2001-525330	20000921
PRAI	JP 1999-269398	A	19990922		
	JP 1999-340322	A	19991130		
	WO 2000-IB1438	W	20000921		

OS MARPAT 134:275749
IT Fever and Hyperthermia
UV **radiation**
(as DNA damaging agent; peptide sequences and methods for inhibiting G2 cell cycle arrest and sensitizing cells to DNA damaging agents)
IT 51-21-8, 5-Fluorouracil 11056-06-7, Bleomycin 15663-27-1, Cisplatin 25316-40-9, Adriamycin **93908-02-2**, **Rebeccamycin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as DNA damaging agent; peptide sequences and methods for inhibiting G2 cell cycle arrest and sensitizing cells to DNA damaging agents)

L6 ANSWER 4 OF 14 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1986-51807 DRUGU P B
TI Kinetics of Topoisomerase Inhibition by VP16-213, VM26, Camptothecin, and Other Agents.
AU Long B H
LO Houston, Texas, United States
SO Proc.Am.Assoc.Cancer Res. (27, 77 Meet., 249, 1986) ISSN: 0197-016X
AV Bristol-Baylor Laboratory, Pharmacology Dept., Baylor College of Medicine, Houston, TX 77030, U.S.A.

LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The kinetics of topoisomerase (II) inhibition by etoposide (VP-16-213), teniposide (VM26), camptothecin, novobiocin, bleomycin, talisomycin gamma **radiation** and **rebeccamycin** was studied in human lung adenocarcinoma cells (A549). Results indicate that the insertion of the 2 subunits of topoisomerase II. . .
ABEX. . . breaks (SSBs) by an entirely different mechanism, also produce similar biphasic elution curves and DNA in the lysis fractions. Gamma **radiation**, **rebeccamycin**, and camptothecin, agents that produce almost no detectable DSBs, produce linear elution curves and no increase in DNA in the. . .
CT [07] **REBECCAMYCIN** *PH; **REBECCAMYCIN** *DM; REBECCAMY *RN; ANTIBIOTICS *FT; CYTOSTATICS *FT; PH *FT; DM *FT

L6 ANSWER 5 OF 14 IFIPAT COPYRIGHT 2003 IFI on STN
AN 10091526 IFIPAT;IFIUDB;IFICDB
TI COMPOSITIONS AND METHODS FOR THE TREATMENT OF CANCER; THALIDOMIDE AND A TOPOISOMERASE INHIBITOR ANTICANCER DRUG SUCH AS IRINOTECAN; REDUCES TOXICITY RELATED SIDE EFFECTS OF ANTICANCER DRUG
INF Barer; Sol, Westfield, NJ, US
Zeitlin; Andrew L., Basking Ridge, NJ, US
Zeldis; Jerome B., Princeton, NJ, US
IN Barer Sol; Zeitlin Andrew L; Zeldis Jerome B
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG PENNIE & EDMONDS LLP, 1667 K STREET NW, SUITE 1000, WASHINGTON, DC, 20006
PI US 2002035090 A1 20020321
AI US 2001-853617 20010514
PRAI US 2000-204143P 20000515 (Provisional)
FI US 2002035090 20020321
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 60
AB . . . The invention further relates to methods of reducing or avoiding adverse side effects associated with the administration of chemotherapy or **radiation** therapy which comprise the administration of thalidomide to a patient in need of such reduction or avoidance.
ACLM . . . consisting of camptothecin, iriniotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED-110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, IST-622, rubitecan, pyrazoloacridine, XR-5000, and pharmaceutically acceptable. . .
. . . of camptothecin, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED- 110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . .
26. A method of reducing or preventing an adverse effect associated with **radiation** therapy, which comprises administering to a patient in need of such treatment or prevention an amount of thalidomide, or a. . . pharmaceutically acceptable prodrug, salt, solvate, hydrate, or elathrate thereof, that is sufficient to reduce an adverse effect associated with the **radiation** therapy.
. . . consisting of camptothecin, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED-110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258,

nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . . . . of camptothecin, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE 1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED-110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . . . . of camptothecin, irinotecan, SN-38, topotecan, 9-aminocamptothecin, GG-211, DX-8951f, saintopin, UCE6, UCE1022, TAN-1518A, TAN-1518B, KT6006, KT6528, ED- 110, NB-506, ED-110, NB-506, **rebeccamycin**, bulgarein, Hoescht dye 33342, Hoechst dye 33258, nitidine, fagaronine, epiberberine, coralyne, beta-lapachone, BC-4-1, and pharmaceutically acceptable prodrugs, salts, solvates, clathrates,. . .

L6 ANSWER 6 OF 14 COPYRIGHT 2003 Gale Group on STN

AN 2003:142804 NLDB
TI ASCO NEWS.(American Society of Clinical Oncology presentations)
SO BIOWORLD Today, (3 Jun 2003) Vol. 14, No. 106.
PB Medical Economics/Thomson Healthcare
DT Newsletter
LA English
WC 2442
TX Exelixis . . . a Phase II trial in 33 patients with bile duct tumors (gall bladder tumors and cholangiocarcinomas) treated with the DEAE-**rebeccamycin** analogue (XL119), who showed encouraging results relative to overall and progression-free survival. The safety profile was manageable and was consistent. . .

GenVec . . . of Gaithersburg, Md., announced preliminary data from the dose-escalation portion of a Phase II study using TNFerade with chemotherapy and **radiation** in patients with locally advanced, inoperable pancreatic cancer. The results showed that TNFerade was well tolerated at the two dose. . . was seen in 11 of 17 evaluable patients. It also announced data from a Phase I trial using TNFerade with **radiation** therapy in patients with soft tissue sarcoma, showing that TNFerade was well tolerated with no dose- limiting toxicity reported. Objective. . .

L6 ANSWER 7 OF 14 TOXCENTER COPYRIGHT 2003 ACS on STN
AN 2002:546164 TOXCENTER
DN CRISP-97-SC06321-17
TI CHEMICAL MODIFICATION OF THE **RADIATION** RESPONSE
AU COOK J A
CS NCI, NIH
CSS U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NATIONAL CANCER INSTITUTE
SO Crisp Data Base National Institutes Of Health.
DT (Research)
FS CRISP
LA English
ED Entered STN: 20021200
Last Updated on STN: 20021200
TI CHEMICAL MODIFICATION OF THE **RADIATION** RESPONSE
AB In the interest of improving cancer treatment, considerable attention has been placed on the modification of **radiation** damage, particularly toward enhancement. A variety of chemotherapy agents have demonstrated **radiation** sensitization and for the past few years we have focused attention on the relatively new agent paclitaxel (Taxol). We have. . . cell lines. Of particular note was the radiosensitization of a human breast adenocarcinoma cell line MCF7. Paclitaxel treatment combined with **radiation** resulted in a **radiation** enhancement ratio (RER) of 1.9. Based on our in vitro data, breast cancer

should be most suitable for combined **radiation** and paclitaxel. We were initially puzzled that human lung adenocarcinoma cells were not radiosensitized by paclitaxel despite the induction of. . . differential exit times in S phase (a radioresistant portion of the cell cycle) among cell types. While not related to **radiation**, we have conducted preliminary pre-clinical studies which show that paclitaxel may be suitably combined with hyperthermia (an experimental cancer treatment. . . designing human clinical trials combining paclitaxel and hyperthermia. We have also initiated studies evaluating gemcitabine, quinocarmycin, and 9-amino camptothecin as **radiation** sensitizers. Preliminary studies show that gemcitabine and 9-amino camptothecin enhance **radiation** sensitivity (enhancement ratios ranging from 1.3-1.5) of human pancreas and lung cancer cell lines. Other chemotherapy agents to be evaluated as **radiation** sensitizers include flavopiridol, **rebeccamycin**, and rhizoxin.

ST . . . Descriptors
camptothecin; taxol; antineoplastic; cell cycle; drug screening ,evaluation; cellular oncology; breast neoplasm; lung neoplasm; neoplasm ,cancer chemotherapy; neoplasm ,cancer **radiation** therapy; combination antineoplastic therapy; neoplasm ,cancer thermotherapy; **radiation** sensitivity; radiosensitizer; tissue ,cell culture; MCF7 cell; CRISP; RPROJ

L6 ANSWER 8 OF 14 USPATFULL on STN
AN 2003:257715 USPATFULL
TI Method, system and knowledge repository for identifying a secondary metabolite from a microorganism
IN Farnet, Chris M., Outremont, CANADA
Staffa, Alfredo, Saint-Laurent, CANADA
Bachmann, Brian O., Westmount, CANADA
McAlpine, James B., Westmount, CANADA
Zazopoulos, Emmanuel, Montreal, CANADA
Zhao, Zhizi, Pierrefonds, CANADA
Wong, Sai Man, Saint-Laurent, CANADA
Desjardins, Nicolas, Pointe-Claire, CANADA
PA Ecopia BioSciences, Inc. (non-U.S. corporation)
PI US 2003180766 A1 20030925
AI US 2003-350341 A1 20030124 (10)
PRAI US 2002-350369P 20020124 (60)
US 2002-398795P 20020729 (60)
US 2002-412580P 20020923 (60)
DT Utility
FS APPLICATION
LREP TIMOTHY BUTTS, 1128 W. 76TH TER APT #6, SHAWNEE, KS, 66214
CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN 20 Drawing Page(s)
LN.CNT 2716
DETD . . . commonly known to effect natural product production such as the addition of DNA damaging agents, selective antibiotics and/or exposure to **radiation** can be used in combination with screening to select for alternate or enhanced natural product production in this invention.
DETD . . . (a known megalomicin producer), Streptomyces cavourensis subsp. washingtonensis NRRL B-8030 (a known chromomycin producer), Saccharothrix aerocolonigenes ATCC 39243 (a known **rebeccamycin** producer), Streptomyces kaniharaensis ATCC 21070 (a known coformycin producer), Streptomyces citricolor IFO 13005 (a known aristeromycin and neplanocin A producer).. . .

L6 ANSWER 9 OF 14 USPATFULL on STN
AN 2003:201367 USPATFULL
TI Compositions and methods for the treatment of inflammatory diseases
IN Jackson, John K., Vancouver, CA, UNITED STATES

Burt, Helen M., Vancouver, CANADA
Dordunoo, Stephen K., Baltimore, MD, UNITED STATES
PI US 2003139353 A1 20030724
AI US 2002-220190 A1 20021203 (10)
WO 2001-CA247 20010228
DT Utility
FS APPLICATION
LREP BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO PARK, CA, 94025
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2283
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . NS6314662; benzoanthracenes, such as saintopinsana UC36; benzophenathidines, such as nitidine, fagaronine and coralyne, intoplicine; indolocarbazoles such as NB506, KT6006 and **rebeccamycin**; anthracyclines such as norpholinodoxorubicin, aclacinomycin and rudofomycin; peptides such as actinomycin, and NUICRF505; benzimidazoles such as Hoechst 33342 and 2,5-substituted. .
.
DETD . . . NS6314662; benzoanthracenes, such as saintopinsana UC36; benzophenathidines, such as nitidine, fagaronine and coralyne, intoplicine; indolocarbazoles such as NB506, KT6006 and **rebeccamycin**; anthracyclines such as norpholinodoxorubicin, aclacinomycin and rudofomycin; peptides such as actinomycin, and NUICRF505; benzimidazoles such as Hoechst 33342 and 2,5-substituted. .
.
DETD . . . states involving hyperproliferating cells (e.g. restenosis, surgical adhesions, rheumatoid arthritis) may be treated with combination therapies involving the coadministration of **radiation** and topoisomerase inhibitors according to this invention.

L6 ANSWER 10 OF 14 USPATFULL on STN
AN 2001:158271 USPATFULL
TI Granulatimide compounds and uses thereof
IN Andersen, Raymond, Vancouver, Canada
Roberge, Michel, Vancouver, Canada
Sanghera, Jasbinder, Vancouver, Canada
Leung, Daniel, Coquitlam, Canada
Piers, Edward, Richmond, Canada
GS Berlinck, Roberto, Sao Carlos, SP, Brazil
Britton, Robert, Vancouver, Canada
PA The University of British Columbia, Vancouver, Canada (non-U.S. corporation)
Kinetek Pharmaceuticals, Inc., Vancouver, Canada (non-U.S. corporation)
PI US 6291447 B1 20010918
AI US 1999-258991 19990226 (9)
PRAI CA 1998-2232074 19980313
CA 1998-2245029 19980814
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.
LREP Sherwood, Pamela J., Parker, David
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1651
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . above, for selectively sensitizing cancer cells. Pentoxifylline has been shown to enhance cisplatin induced killing of p53-MCF-7 cells 30-fold and **radiation** induced killing of p53-A549 human lung adenocarcinoma cells 5-fold. For example, see Russell et al. (1995)

Cancer Res. 55:1639-1642; Powell. . .
DETD . . . in association with treatment of cancer cells, more particularly in combination with cytotoxic therapy directed at said cancer cells; e.g. **radiation** treatment, chemotherapeutic drugs, etc.
DETD Synthesis of Compounds Related to **Rebeccamycin**
CLM What is claimed is:
19. The method according to claim 18, wherein said cytotoxic therapy is **radiation** treatment.

L6 ANSWER 11 OF 14 USPATFULL on STN
AN 91:102299 USPATFULL
TI BMY-41950 antitumor antibiotic
IN Schroeder, Daniel, Higganum, CT, United States
Lam, Kin S., Cheshire, CT, United States
Mattei, Jacqueline, East Haven, CT, United States
Hesler, Grace A., Branford, CT, United States
PA Bristol-Myers Company, New York, NY, United States (U.S. corporation)
PI US 5073633 19911217
AI US 1990-608773 19901105 (7)
RLI Division of Ser. No. US 1990-482364, filed on 20 Feb 1990, now patented, Pat. No. US 5015578 which is a continuation-in-part of Ser. No. US 1989-327929, filed on 23 Mar 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: Webber, Pamela S.
LREP Yang, Mollie M., Morse, David M.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 536
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM The antitumor antibiotic named **rebeccamycin** is disclosed in U.S. Pat. No. 4,552,842 as being produced by fermentation of Nocardia aerocolonigenes ATCC 39243. **Rebeccamycin** has the structural formula ##STR3## The producing organism has recently been reclassified as Saccharothrix aerocolonigenes (J. Antibiot. 40:668-14 678, 1987).
DETD . . . to include other BMY-41950-producing strains or mutants of the described organisms which can be produced by conventional means such as x-**radiation**, ultraviolet **radiation**, treatment with nitrogen mustards, phage exposure and the like.

L6 ANSWER 12 OF 14 USPATFULL on STN
AN 91:38414 USPATFULL
TI BMY-41950 antitumor antibiotic
IN Schroeder, Daniel, Higganum, CT, United States
Lam, Kin S., Cheshire, CT, United States
Mattei, Jacqueline, East Haven, CT, United States
Hesler, Grace A., Branford, CT, United States
PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)
PI US 5015578 19910514
AI US 1990-482364 19900220 (7)
RLI Continuation-in-part of Ser. No. US 1989-327929, filed on 23 Mar 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: Webber, Pamela S.
LREP Morse, David M.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 551
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM The antitumor antibiotic named **rebeccamycin** is disclosed in U.S. Pat. No. 4,552,842 as being produced by fermentation of Nocardia aerocolonigenes ATCC 39243. **Rebeccamycin** has the structural formula ##STR3## The producing organism has recently been reclassified as Saccharothrix aerocolonigenes (J. Antibiot. 40: 668-678, 1987).
SUMM . . . to include other BMY-41950-producing strains or mutants of the described organisms which can be produced by conventional means such as x-**radiation**, ultraviolet **radiation**, treatment with nitrogen mustards, phage exposure and the like.

L6 ANSWER 13 OF 14 USPATFULL on STN
AN 86:4983 USPATFULL
TI Process for preparing 4'-deschlororebeccamycin
IN Matson, James A., Fayetteville, NY, United States
PA Bristol-Myers Company, New York, NY, United States (U.S. corporation)
PI US 4567143 19860128
AI US 1985-690271 19850318 (6)
RLI Division of Ser. No. US 1984-646673, filed on 4 Sep 1984, now patented, Pat. No. US 4524145
DT Utility
FS Granted
EXNAM Primary Examiner: Tanenholtz, Alvin E.; Assistant Examiner: Weimar, Elizabeth C.
LREP Morse, David M.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 628
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM The novel compound of the present invention is related in structure to the antitumor agent, **rebeccamycin**, disclosed and claimed in co-pending application Ser. No. 461,817 filed Jan. 28, 1983, now U.S. Pat. No. 4,487,925 the entire disclosure of which is hereby incorporated by reference. **Rebeccamycin** has the formula ##STR1## and is obtained by cultivating Nocardia aerocolonigenes.
SUMM . . . U.S. application Ser. No. 461,817 filed Jan. 28, 1983 now U.S. Pat. No. 4,487,925 as being the producing organism for **rebeccamycin**. The present applicant has discovered that during cultivation of this microorganism there is co-produced along with **rebeccamycin** the 4'-deschlororebeccamycin product of the present invention. This preferred producing microorganism, designated strain C38,383-RK2, was isolated from a soil sample. . .
SUMM . . . to include other 4'-deschlororebeccamycin-producing strains or mutants of the said organism which can be produced by conventional means such as x-**radiation**, ultraviolet **radiation**, treatment with nitrogen mustards, phage exposure, and the like.
SUMM . . . the serial two-fold agar dilution method. The results are shown in Table 5 below in comparison with the activity of **rebeccamycin**
.
SUMM TABLE 5

Antibacterial Activity of 4'-Deschlororebeccamycin

Organism		Minimum Inhibitory Concentration (MIC) (mcg/ml) **Rebeccamycin**	4'-Deschloro-**rebeccamycin**
S. pneumoniae	A9585	>125	32

S. pyogenes A9604	>125		32
S. faecalis A20688	8		16
S. aureus A9537	0.5		2
M. luteus A9547	0.5		1

S.. . .

SUMM . . . on P-388 Leukemia

Material	Dose, IP mg/kg/inj	MST Days	MST % T/C	Average weight change, day 5	Sur-vivors gm day 10
Rebeccamycin					
	512	17.0	155	-1.4	6/6
	256	15.0	136	-0.3	6/6
	128	14.5	132	0.2	6/6
	64	15.0	136	0.3	6/6
	32	13.0	118	-0.6	6/6
	16	15.0	136	-0.8	6/6
4'-Deschloro-					
	512	15.5	141	-1.0	4/4
rebeccamycin					
	256	15.0	136	-1.5	4/4
	128	17.5	159	-0.6	4/4
	64	15.0	136	-0.8	4/4
	32	15.5	141	-0.8	4/4

. . .

L6 ANSWER 14 OF 14 USPATFULL on STN
AN 85:35892 USPATFULL
TI 4'-Deschlororebeccamycin pharmaceutical composition and method of use
IN Matson, James A., Fayetteville, NY, United States
PA Bristol-Myers Company, New York, NY, United States (U.S. corporation)
PI US 4524145 19850618
AI US 1984-646673 19840904 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Brown, Johnnie R.
LREP Morse, David M.
CLMN Number of Claims: 3
ECL Exemplary Claim: 3
DRWN No Drawings
LN.CNT 627
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The novel compound of the present invention is related in structure to the antitumor agent, **rebeccamycin**, disclosed and claimed in co-pending application Ser. No. 461,817 filed Jan. 28, 1983, the entire disclosure of which is hereby incorporated by reference. **Rebeccamycin** has the formula ##STR1## and is obtained by cultivating Nocardia aerocolonigenes.

SUMM . . . strain is that disclosed in U.S. application Ser. No. 461,817 filed Jan. 28, 1983 as being the producing organism for **rebeccamycin**. The present applicant has discovered that during cultivation of this microorganism there is co-produced along with **rebeccamycin** the 4'-deschlororebeccamycin product of the present invention. This preferred producing microorganism, designated strain C38,383-RK2, was isolated from a soil sample. . .

SUMM . . . to include other 4'-deschlororebeccamycin-producing strains or mutants of the said organism which can be produced by conventional means such as x-**radiation**, ultraviolet **radiation**, treatment with nitrogen mustards, phage exposure, and the like.

SUMM . . . the serial two-fold agar dilution method. The results are shown in Table 5 below in comparison with the activity of **rebeccamycin**
.

SUMM TABLE 5

Antibacterial Activity of 4'-Deschlororebeccamycin

Organism		Minimum Inhibitory Concentration (MIC) (mcg/ml) Rebeccamycin	4'-Deschloro-rebeccamycin
S. pneumoniae	A9585	>125	32
S. pyogenes	A9604	>125	32
S. faecalis	A20688	8	16
S. aureus	A9537	0.5	2
M. luteus	A9547	0.5	1

S.. . .

SUMM . . . on P-388 Leukemia

Material	Dose, IP mg/kg/inj	MST Days	MST % T/C	Average weight change, day 5	Surgm vivors day 10
Rebeccamycin					
	512	17.0	155	-1.4	6/6
	256	15.0	136	-0.3	6/6
	128	14.5	132	0.2	6/6
	64	15.0	136	0.3	6/6
	32	13.0	118	-0.6	6/6
	16	15.0	136	-0.8	6/6
4'-Deschloro-					
	512	15.5	141	-1.0	4/4
rebeccamycin					
	256	15.0	136	-1.5	4/4
	128	17.5	159	-0.6	4/4
	64	15.0	136	-0.8	4/4
	32	15.5	141	-0.8	4/4

. . .

=>